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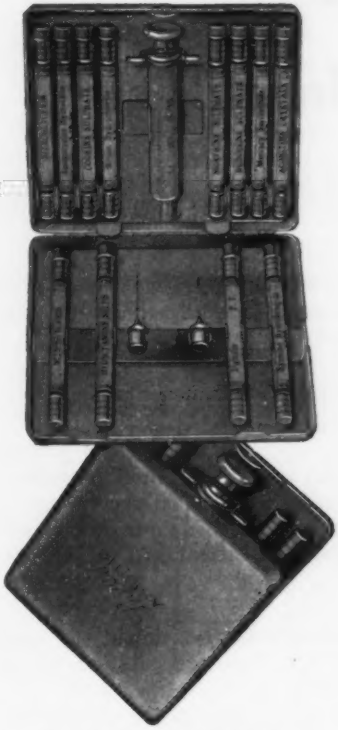

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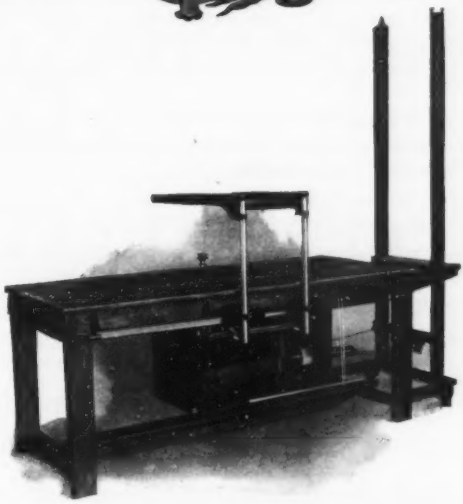

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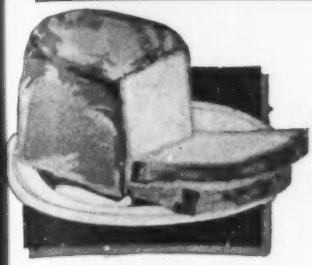

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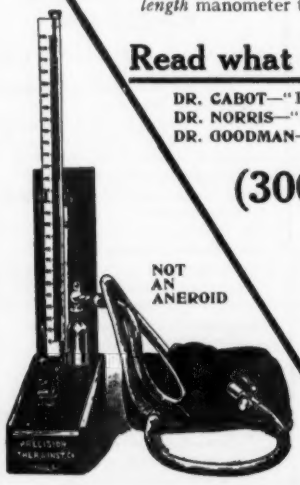

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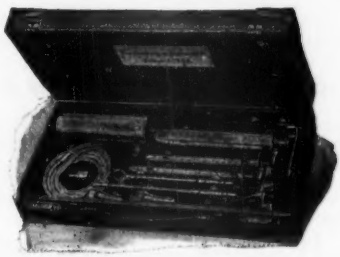

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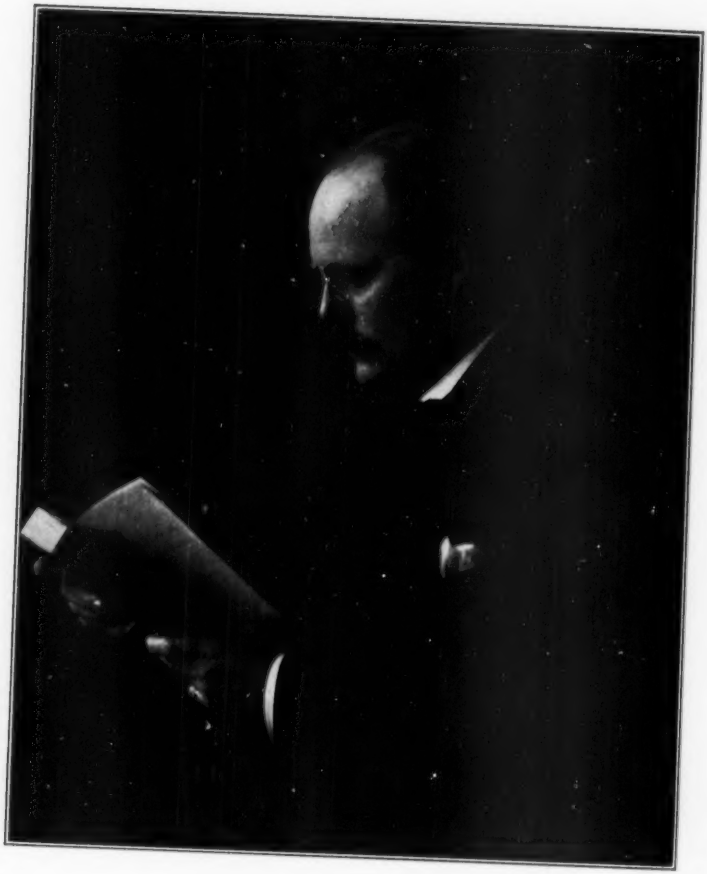

CLARENCE JOHN BLAKE, M.D.

CLARENCE JOHN BLAKE, M.D.

I HAVE been asked to write a few lines about the late Clarence John Blake, M.D., of Boston, Massachusetts. I shall not attempt to enumerate the offices which he held, the names of the societies of which he was a member or the papers which he wrote upon medical or other subjects. For all of these things I must refer to the records, which are compiled and kept for reference, concerning the lives of prominent men.

My endeavor will be to convey the impression which certain of Dr. Blake's characteristics made upon me during a fairly intimate professional companionship covering some twenty odd years.

First and foremost, I wish to speak of his great and unfailing kindness to his patients, whether hospital or private. Their welfare and relief were the *only* things which he thought about. No time (whether night or day) and no trouble or inconvenience were ever allowed to weigh for a moment against a possible benefit to the patient, and he gave himself absolutely, both brain and body, to their service. Thousands of his patients are today lamenting his loss, not only because they have lost a skilled physician who helped their ailments, but because they feel that they have also lost a friend who took an intense interest in all that affected them and to whom they could go for advice and counsel on any subject, whether medical or non-medical, with the certainty that he would give both time and thought to an endeavor to help them. This was a marked characteristic of Dr. Blake, and I wish to lay great stress upon it.

His intelligence was very keen, his mind very active. He saw more, and more quickly, than other men, and what he saw suggested all sorts of possibilities to him, of which he was very quick to make use. This was a great help to him in original investigation.

It so happened that Dr. Blake was among the first in this country who made a specialty of otology after the invention of the forehead mirror had revolutionized that branch of medicine by allowing the doctor to see into the ear. He therefore belongs to those who *created* the treatment for aural diseases, and he took advantage of his great opportunities and did his full share toward the rapid advances which were then made. He studied for a long time under Prof. Politzer, in Vienna, and was selected by him

to be his assistant, a great honor, which showed how highly he was esteemed by Prof. Politzer; and he had a very enviable international reputation during his whole life, so that when his pupils went to Europe in after years the first question asked, as soon as it was known that they came from the Harvard Medical School, was: "How is Dr. Blake? What is he doing? Is there anything new scientifically from him?"

He was loth to cause pain and was exceedingly deft and skilful with his fingers, and he taught all who came under his tutelage how to perform all the painful and unpleasant things which an aurist has to do, with a minimum of pain and distress to the patient. This also I wish to lay stress upon, although it is a small thing, for it saved the patient from untold misery.

I first knew Dr. Blake when I applied as a volunteer during his service at the Massachusetts Charitable Eye and Ear Infirmary, and he was kindness itself in explaining and showing me all that pertained to the anatomy of the ear and nose and to the diagnosis and treatment of their diseases. He was a wonderful and most interesting teacher, and no assistant or house officer has ever worked with him or under him without learning more from him than he could ever have learned from all the text-books in creation. I can freely say that he taught me the most of what I know about otology, although I often did not agree with him as to treatment. I knew him first as an assistant, then as a colleague, and for years he used to send certain cases to me for treatment, and we consulted together about them. If I was worried about a serious and dangerous case I always went to him for advice, and I have never done so, whether in the middle of the night or at meal times, or after his long office hours were over, that he did not give his best thought to the case; and if it seemed necessary he would go at once (whether by night or day) to see the case with me. He never failed me, and was never too tired to help a patient who was in pain or danger.

Dr. Blake and I differed many times and about many things, but my respect for his unfailing kindliness, his quick perceptions and his alert and resourceful mind was very great, and he certainly did a great deal for both the scientific and the practical side of otology.

HENRY LEE MORSE, M.D.

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ORIGINAL ARTICLES

ROENTGEN-RAY INTOXICATION: DISTURBANCES IN METABOLISM PRODUCED BY DEEP MASSIVE DOSES OF THE HARD ROENTGEN RAYS.

By C. C. Hall

AND

G. H. Whipple, M.D.,

SAN FRANCISCO, CALIFORNIA.

(From the George Williams Hooper Foundation for Medical Research, University of California Medical School, San Francisco.)

This paper deals with the general constitutional reaction which follows prolonged exposures to the roentgen rays of the Coolidge tube. The experiments tabulated below give data to show the increase in nitrogen elimination and in blood non-protein nitrogen which precedes the fatal intoxication. Some of the interest centers upon the intestinal epithelium which gives evidence of injury, and it is possible that this injured epithelium may be responsible in large measure for the clinical symptoms of vomiting, diarrhea and prostration. The parenchymatous organs, with the exception of the spleen, give no evidence of any specific injurious action of the roentgen rays. We can submit no evidence for any specific action of the roentgen rays upon cell ferments, but the remarkable specific action of the roentgen rays upon certain cells speaks for an individual peculiarity of these cells apart from their autolytic ferments. It may be that the cell ferments are wholly responsible for the cell autolysis and disappearance once the primary specific cell injury has been effected by the roentgen rays.

We became interested in this subject following a study of roentgen-ray burns. The long latent period of the roentgen-ray burn and the lack of systemic reaction have never been satisfactorily explained, nor can we bring any sufficient explanation at this time. Much more is known about the intoxication of the common heat burn, and the evidence is pretty conclusive that body protein in the burned area is injured in such a manner that toxic split products are formed and absorbed into the body. If these toxic protein split products are in sufficient amount there will result a fatal systemic intoxication.

That roentgen rays were capable of producing burns was noted very soon after their discovery, probably first reported by Leppin.[31] Since that time the records have multiplied into the hundreds. The late results of roentgen-ray burns and irritations which may result in cancer growth began to appear. Soon it was pointed out by Albers-Schönberg[1] and Halberstaedter[18] that sterilization could be effected by the roentgen rays, and must be guarded against.

Constitutional reactions following the roentgen-ray treatment began to be noted. Perhaps the first on record is that reported by Walsh.[55] The danger of these systemic reactions has been repeatedly emphasized by Edsall and his collaborators.[12 14 15]

It is safe to state that the frequency of these constitutional reactions is on the increase, and we wish to point out the danger of such reactions. The Coolidge tube is mainly responsible for this because by means of the improved tube it is now possible to administer "massive" doses (Cole[8 9]) to structures below the skin and by "cross-fire" escape the danger of a burn. The "hard rays" of a Coolidge tube with a wide spark gap have much greater capacity to cause the tissue injury which is responsible for the constitutional reaction than had the older tubes. (Note Table XV.)

The general systemic or constitutional reaction varies considerably as reported by various writers who have observed these reactions in their patients following roentgen-ray treatment. There is much variation as regards the dosage of the roentgen rays, filters used, spark gap, etc. The reaction may begin shortly after the irradiation or be delayed for days. As usually described it consists of loss of appetite, malaise, nausea and vomiting. Diarrhea may be severe and prostration may be profound. Some authors record slight fever and others a slow, weak pulse, with subnormal temperature. In the University of California Hospital not long ago two boys were treated for ringworm of the scalp, and their mother reported that after going home they became very sick and vomited for several hours.

The general constitutional reaction which follows the use of large doses of the roentgen rays is of considerable interest because of a certain resemblance to intoxications in dogs caused by proteose injections. Both may be regarded as true "non-specific" reactions

associated with much destruction of body protein and these intoxications are to be compared with other "non-specific" intoxications: for example, intestinal obstruction and acute pancreatitis. Therefore a study of the intoxication due to treatment by the roentgen rays takes on a new interest because it is one of the "non-specific" intoxications. Bacteria and specific toxins and endotoxins or antibodies cannot possibly be concerned. It is practically sure that all specific infections and intoxications are associated with a certain unknown "non-specific" factor of disease, a proper understanding of which may be obtained by careful study of all types of pure "non-specific" intoxication. The roentgen-ray intoxication is an important member of this group of pure "non-specific" intoxications.

Many papers deal with this constitutional reaction: Edsall and Pemberton,[14] [15] Lange[30] and Pfahler.[42] Pfahler believes that the symptoms are due to poor ventilation of the roentgen-ray room, causing the patient to inhale certain gases produced in the air by the action of the high-tension current. In a slightly different form this theory was also advanced by Wilbert,[59] although the two authors differ as to the exact nature of the noxious gases produced. This argument may be dismissed without comment.

Lange maintains that the reaction is the result of an acidosis resulting from cellular degeneration or from increase in catabolic cellular activity. He submits no analyses of blood or expired air to support this claim. On this theory he attempts to counteract the constitutional effects with doses of sodium bicarbonate.

Edsall and Pemberton advanced a theory which we believe to be more nearly correct. They noted that roentgen rays sometimes produced a constitutional reaction which they ascribed to an acute intoxication. They state, as their belief: "The tissue destruction accomplished by roentgen rays undoubtedly involves chiefly tissues especially rich in nucleoprotein. The decomposition products of this form of protein are expecially rich in substances that are more or less toxic and difficult to metabolize and excrete." Further: "The intoxication is not dependent directly upon alterations in the excreting power of the kidneys because examinations of the urine of two patients showed no evidence of irritation of the kidneys. It is, however, probable in many cases, after a time, that the kidneys do become overtaxed by the added labor thrown upon them and their excretory power fails to a greater or less degree, and this may increase the toxic symptoms."

The source of these toxic products and the mechanism by which the roentgen rays produce their physiological action still remain subjects of dispute. As to the former, several theories have been advanced.

1. It has been claimed by Linser and Sick,[34] Engel[16] and others that the roentgen rays produce a roentgen toxin in the blood which might be responsible for the increased protein destruction. As

might be expected, it is impossible to demonstrate any such roentgen toxin in the blood, and the experiments submitted are not controlled. Many toxic substances introduced into the blood are removed so rapidly as to defy detection, so a negative result gives no assurance that a powerful toxin may not have been present in the blood.

2. It has been claimed by Heile[19] and others that the destruction of the white blood cells resulted in the release of a great store of powerful intracellular enzymes, which then attacked various tissues to produce the protein degradation noted. But we now know of powerful anti-enzymes which are constantly present in the blood during life.

3. It has been suggested by Baerman and Linser,[2] Rosenstern,[51] Edsall[12] and others that roentgen rays may have a stimulating effect on enzyme activity in general and particularly in these cases on the enzymes which produce tissue autolysis. Edsall, acting on this hypothesis, concluded that roentgen rays might be of value in the treatment of unresolved pneumonia. He used them in a number of such cases and reports excellent results—Edsall and Pemberton.[14]

Much work has been reported on the effect of roentgen radiation on ferment activity, and this might be cited to substantiate the last-mentioned theory. There is also a relatively large literature on the effect on enzymes produced by radium emanations, and it is now generally accepted that the two kinds of radiant energy are practically identical in their physiological action. Wohlgemuth[60] showed that radium rays stimulate the autolysis of tuberculous lung tissue *in vitro*. Neuberg[40] demonstrated that fresh carcinoma tissue autolyzes more rapidly *in vitro* under the influence of radium emanation than does a control not so exposed or similar tissue which had first been cooked before being rayed. He also makes the statement that radium inactivates trypsin, rennin, pepsin, etc., and believes that this furnishes a key to its action on cancer tissue; that it causes destruction of all intracellular ferments which bring about anabolic processes, while those producing autolysis are unaffected. In modern terminology he believes radium acts by destruction of anti-enzymes.

The best work on the effect of roentgen rays on ferments is that of Richards,[45] in which he demonstrates that a short radiation with roentgen rays accelerates enzymatic activity while a longer radiation inhibits it. This holds for the digestion of egg albumen by pepsin and of starch by diastase. "Between these two strengths," he says, "lies a point at which the radiation is non-effective." He does not believe, however, that the effects of radiation on enzymes, which he has demonstrated, are sufficient to account completely for its action on cells. On the other hand, Richter and Gerhartz[47] maintain that the effects noted by other authors—at times an increase, at others a decrease in ferment activity—are due to experimental errors. They claim that roentgen rays have absolutely no

effect on ferments and that theories which attempt to explain the biological action of roentgen rays through the influencing of enzymatic processes, "auf sehr schwachen füssen stehen." A very interesting review of this whole field is given by Richards.[46]

One other feature seems worthy of attention as the attempt has been made to charge the constitutional effects following prolonged exposure to roentgen rays to the production of a nephritis. That roentgen rays produce a nephritis has been claimed by many workers —Linser and Helber,[33] Rosenstern,[51] Warthin[56] and others. On the other hand, negative findings are reported by Buschke and Schmidt,[7] Krause and Ziegler[28] and others, and several of those who have reported positively admit that the renal trouble is very transitory. Careful examination of the kidneys of our series of animals at autopsy and of the microscopic sections has convinced us that if there is renal injury it is of a relatively slight grade and is not a constant finding. Indeed, the fact that its existence is under dispute demonstrates that it must be of a very slight grade. Perhaps we may assume that the renal epithelium like other body cells may be injured by the roentgen rays, but this injury cannot be extensive because function is but little disturbed and the anatomical changes when present are admittedly slight.

Numerous contributions are to be found in medical literature dealing with metabolism studies of persons treated by the roentgen rays or by radium. Almost all of these reports deal with patients suffering from acute or chronic leukemia. For a review of this literature we wish to refer to the excellent papers of Keymling[25] and Murphy and Means and Aub.[38] It is best to summarize some of the outstanding facts which we must keep in mind during the discussion of the experiments given below.

Leukemic patients show an increase in basal metabolism and usually a negative nitrogen balance. The uric acid of the blood is usually above normal and the endogenous uric-acid elimination usually increased. There may be retention of phosphates. The changes are more striking in acute leukemia and may be quite variable in chronic leukemia.

Treatment with the roentgen rays may not have any definite effect on leukemia cases (Goodall[17]), but usually causes an increased elimination of nitrogen, uric acid and purin bases. The fall in the leukocyte curve does not bear any constant relationship to the elimination of nitrogenous substances.

Most of the work done with the roentgen rays concerned abnormal human beings: leukemia, Hodgkin's disease and the like, but some work has been done upon normal animals and human beings.

Quadrone[44] studied one guinea-pig and six rabbits. His results were not uniform, but in most cases he got a slight increase in the P_2O_5 output following radiation. Bloch[5] studied the metabolism of one man rayed for chronic eczema. He found that the rays caused

increased uric-acid output in the urine, also an increased output in the P_2O_5 and purin bases. Benjamin and v. Reuss[3] rayed one dog and studied his metabolism. Their animal developed constitutional symptoms similar to those of our series and showed an increase in N elimination beginning immediately and lasting several days, transient increase in P_2O_5 output and very transient appearance of cholin in the blood. Lommel[35] conducted metabolism observations on three young dogs with similar results, and Linser and Sick[34] studied five human patients under roentgen treatment for various skin diseases. None of their patients became sick but all showed an increase in urinary N of 2 or 3 grams while their uric-acid output tripled in some cases, and the purin bases also increased. They repeated the experiment on one normal dog, with similar results.

Method.

Dogs were used in all experiments, and unless otherwise noted in the charts were in normal condition. The dogs were usually starved for two or three days before the urinary collections were initiated. Dogs were kept at all times in large metabolism cages constructed with sharply pitched floors to facilitate the complete collection of urine. All fluids were given by stomach tube unless the dog was vomiting constantly, when the fluids were placed in a cup fixed in the cage. In such experiments the nitrogen analysis includes the vomitus, but it is known from many analyses that such vomitus contains only a trace of nitrogen. Every day at the same hour the dog was catheterized, the urinary bladder rinsed out and the fluids given by stomach tube, the cage washed and all cage urine measured. The cage urine, cage washings and catheter specimens were combined, diluted to a unit volume and duplicate analysis of samples for nitrogen made by the Kjeldahl method.

When the dog had reached a level of nitrogen elimination under these conditions the animal was given morphin, to prevent restlessness, followed by the roentgen-ray treatment. The Coolidge tube was used in all cases and the distance of the anticathode from the dog's body was in all cases ten inches. The roentgen-ray dose was given on each side of the abdomen and on each side of the thorax, one-fourth of the total dose on each area. Some preliminary work was necessary to determine the roentgen-ray dose necessary to produce skin injury or a constitutional reaction. It was soon found that the thick hairy dog's skin was very much more resistant than the human skin. It is probable that the dog is more resistant to the constitutional effect of the roentgen rays but the data available is scanty. Observations are usually recorded on diseased and abnormal human beings, and there is usually no record of the spark gap, which we shall see is an important factor. Aluminum filters (2 mm.) were usually used unless otherwise noted for the systemic reaction, but not used when a dermatitis was desired.

Experimental Observations.

The first two experiments given below (Tables I and II) show the result of a fatal dose of the roentgen rays. The first dog was given a very large dose (500 ma. minutes), probably over two lethal doses as contrasted with the second dog (Table II), which was given only 200 ma. minutes—just about the minimum lethal dose. Table V shows an experiment in which a dose of 200 ma. minutes was not fatal and only caused a minimal clinical reaction. It is noteworthy that death occurred in both these experiments (Tables I and II) on the fourth day whether the dose was large or small. In the first experiment with the larger dose the nitrogen elimination is greater and the clinical reaction was more prompt, but, as a rule, the fourth day brings the maximum intoxication, followed by death or recovery. Exceptions to this will be discussed later.

Delay in the onset of clinical symptoms is well illustrated by Table II. This dog for two days was perfectly normal so far as any clinical signs could show—active and vigorous, with no gastro-intestinal symptoms. Vomiting and diarrhea appeared on the third day in spite of the fact that the dog received only water by the stomach tube. Prostration and intoxication were striking on the fourth day, and it is certain that the dog would have died late on the fourth day. This peculiar latent period must be explained by any hypothesis which may be advanced to solve the puzzle of roentgen-ray intoxication.

Autopsy findings are mainly negative. One notes that the spleen is usually smaller than normal and the lymphocytes are less numerous than normal. The heart, lungs, pancreas and liver are negative. The kidneys may show a little cloudy swelling and perhaps a few casts. The gastro-intestinal tract usually shows more or less engorgement of its capillaries and a congested mottled mucous membrane. This congestion is least in the stomach and usually most intense in the duodenum and jejunum. At times it may be most intense in the colon and ileum. There are no ulcers, but some signs of epithelial necrosis. This capillary engorgement must explain the blood-tinged diarrhea which is such a constant feature of the fatal intoxication in dogs.

TABLE I.—18-45—ROENTGEN RAY, LETHAL DOSE.

Date.	Weight, pounds.	Urine, c.c.	Nitrogen, grams.	Diet.	Remarks.
Oct. 1	23.93	460	2.38	400 c.c. water	Dog normal; slight cystitis.
2	23.37	520	2.52	400 "	
3	23.00	440	....	400 "	
3	Roentgen ray—500 ma. min., 2 mm. aluminum filters, spark gap 9 ins.				
4	22.00	545	4.20	400 c.c. water	Dog dull.
5	21.81	550	5.88	400 "	Vomiting.
6	20.62	410	7.34	400 "	Dog very sick; vomitus; blood N. P. N. = 50 mg.
7	Dead	655	4.76	....	Much bloody diarrhea.

Autopsy (Dog 18–45, Table I). Serous surfaces dry. Blood clots soft and dark red. Heart, lungs, spleen, liver, kidneys, pancreas are all normal. Bladder and urethra show a diffuse inflammation of the mucosa. The gastro-intestinal tract throughout shows congestion and a peculiar mottled appearance conspicuous in the small intestine, which is tightly constricted. There are no ulcers of any description. The mucous membrane of the stomach and intestine is velvety and engorged.

Microscopic Sections. Pancreas, kidney and liver show nothing but moderate capillary engorgement. Spleen is not decreased in size, its Malpighian bodies are well preserved and the pulp is engorged. Mucosa of the intestinal tract unfortunately shows much portmortem change, but it is evident that an unusual change has taken place in the epithelium covering the villi and lining the crypts. This epithelium has almost completely disappeared by autolysis, leaving empty crypts. There is but little leukocytic or inflammatory reaction, so it is probable that this autolysis happened after death, but we cannot attribute this change to the usual postmortem autolysis which begins in the tips of the villi and spreads downward involving all structures. This autolysis involves the epithelial cells of the mucous membrane and is to be referred perhaps to the peculiar effect of the roentgen rays. It is known that roentgen-ray exposure of cancer epithelium causes great increase in its speed of autolysis *in vitro*. It is of some interest that the pancreatic cells which are rich in ferments are but very little changed in this case.

TABLE II.—18–69—ROENTGEN RAY, LETHAL DOSE.

Date.	Weight, pounds.	Urine, c.c.	Nitrogen, grams.	Diet.	Remarks.
Nov. 25	21.75	455	2.69	400 c.c. water	Dog normal.
26	21.19	383	2.24	400 "	
27	20.87	351	1.74	400 "	Blood N. P. N. = 31 mg.
28	20.43	271	1.60	400 "	
28	Roentgen ray—200 ma. min., 2 mm. alumi				num filter, spark gap 9 inches.
29	20.13	352	2.69	400 c.c. water	Dog normal.
30	19.87	402	2.41	200± "	Dog normal.
Dec. 1	19.50	501	2.52	200± "	Vomitus; diarrhea; dog active.
2	18.31	1025	2.97	200± "	Dog sick; vomitus; diarrhea.
2	Sacrifice—Blood non-protein nitrogen = 59 mg.				

Autopsy (Dog 18–69, Table II). Thorax, heart, lungs, thymus normal. Liver, kidneys, pancreas moderately engorged. Spleen about two-thirds normal size and hard. Mesenteric lymph glands hard, red and translucent. Stomach normal. Duodenum slightly engorged. Small intestine almost normal, except for small patches of congestion. Submucosa appears red. Intestine not ulcerated.

Microscopic Sections.—Thymus, pancreas, liver and kidneys are negative. Spleen shows some yellow granular pigment. Mesenteric lymph gland shows many polymorphonuclear leukocytes in its

sinuses. Intestinal mucosa shows no acute inflammation. Epithelium seems normal. Goblet cells and mucus are conspicuous.

Table III is to be contrasted with the two preceding experiments. In this experiment the *spark gap* is only six inches as compared with nine inches in the first two experiments. We may say that the minimum lethal dose with a nine-inch spark gap is about 200 to 210 ma. minutes and with a six-inch spark gap is about 450 to 500 ma. minutes. The nine-inch spark gap, of course, represents an electric current of much higher voltage and the constitutional effect of such a current is much greater than a lower voltage current with smaller spark gap.

The dog was profoundly intoxicated on the fourth day and death seemed very probable. An intravenous injection of hypertonic glucose solution containing calcium lactate was given, with temporary benefit. There was a remarkable retention or sparing of nitrogen on the following day, as shown by the urinary nitrogen. An identical procedure was carried out forty-eight hours later. The dog was sacrificed on the seventh day, as there was no hope of recovery from the intoxication.

The blood non-protein nitrogen was unusually high in this animal and an explanation is given by the autopsy. There was conclusive evidence of septicemia, with pulmonary and submucous ecchymoses, small infarct in adrenal and tiny focal abscesses in the kidneys. There were areas of inflammatory reaction in the gastric and intestinal mucous membrane. We may assume that epithelial injury associated with the profound systemic intoxication allowed the intestinal bacteria to invade the mucous membranes and blood stream.

TABLE III.—17–172—ROENTGEN RAY, LETHAL DOSE.

Date.	Weight, pounds.	Urine, c.c.	Nitrogen, grams.	Diet.	Remarks.
April 1	33.00	435	2.91	400 c.c. water 100 gm. sugar	Dog normal.
2	32.25	390	2.80	"	
3	31.75	462	3.02	"	
3	Roentgen ray—500 ma. min., 2 mm. aluminum filter, spark gap 6 inches.				
4	30.81	370	3.53	400 c.c. water 100 gm. sugar	Dog normal.
5	30.00	622*	3.36	"	Slight vomitus.
6	29.00	653*	5.26	"	Much vomitus; dog very sick.
7	27.44	977*	7.73	400 c.c. water in cage	570 c.c. glucose solution, 10 per cent. containing 0.2 gm. calcium lactate.
8	27.00	743*	2.58	400 c.c. water in cage	Diarrhea; little vomitus.
9	26.70	609*	9.41	400 c.c. water in cage	550 c.c. glucose solution, 10 per cent. containing 0.2 gm. calcium lactate.
10	26.50	818*	3.72	....	Profound intoxication.
10	Sacrifice—Blood non-protein nitrogen = 201 mg.				

* Urine contains vomitus.

Autopsy (Dog 17–172, Table III). Heart and thorax normal. Lungs are specked with small hemorrhagic areas not over 1 to 2 mm. in diameter. Spleen and liver negative. Kidneys show a few opaque specks, probably abscesses in cortex and pyramids. Pancreas and thyroid somewhat congested. Bladder shows a catarrhal cystitis. Stomach and intestines show occasional submucous hemorrhages.

Microscopic Sections. Lung shows areas of hemorrhages and a few patches of leukocytic exudate, involving only small groups of acini. Spleen shows much blood pigment and a decrease in pulp cells. Malpighian bodies are not decreased in size but leukocytes are scanty in pulp. Liver shows a little cloudy swelling. Adrenal shows a small-sized infarct about 3 mm. in diameter. Kidneys show a very few tiny linear abscesses. The tubular epithelium shows some degeneration but no necrosis. Stroma normal. There are a few hyaline casts. Testes contain spermatozoa. Stomach shows definite inflammatory reaction of mild grade in its mucosa, with invasion of polymorphonuclear leukocytes. There is slight edema, but no obvious epithelial necrosis. Small intestine shows occasional small areas of early inflammation.

TABLE IV.—18–71—ROENTGEN RAY, LETHAL DOSE.

Date.	Weight, pounds.	Urine, c.c.	Nitrogen, grams.	Diet.	Remarks.
Dec. 4	13.87	306	2.24	300 c.c. water	Dog normal.
5	13.43	338	2.24	300 "	
6	13.19	331	2.46	300 "	
6	Roentgen ray—210 ma. min., 2 mm. aluminum filter, spark gap 9 inches.				
7	12.75	295	2.43	300 c.c. water	Dog normal.
8	12.38	361	2.55	300 "	Dog normal.
9	11.87	401	3.64	300 "	Vomiting.
10	11.38	295	5.04	200 "	Vomiting; black diarrhea; dog very sick.
11	11.19	226	3.72	265 "	Clinical improvement.
12	11.06	206	3.70	230 "	Clinical improvement.
13	10.87	262	3.47	200 "	No diarrhea.
14	10.31	232	3.14	200 "	Diarrhea.
15	10.19	225	3.14	325 "	Diarrhea marked.
16	Found dead—vomitus in cage.				

Table IV illustrates a temporary recovery from the general intoxication following a dose of 210 ma. minutes with nine-inch spark gap. As usual the dog was profoundly intoxicated on the fourth day following the roentgen-ray treatment. There were prostration, vomiting and bloody diarrhea. Then came a period of clinical improvement for three days, followed by two days of intoxication and death.

It is clear from the autopsy that this dog was about to recover from the specific roentgen-ray intoxication which reached its maximum as usual on the fourth day, just short of a lethal intoxication. The

autopsy showed many ecchymoses in the liver, kidneys and intestinal mucosa. The liver showed typical focal hyaline necroses probably not over forty-eight hours of age. There was epithelial degeneration in the kidneys. The mucosa of the small intestine showed an early inflammatory reaction, with slight edema and inwandering of polymorphonuclear leukocytes. It is possible that intestinal bacteria gained entrance to the blood stream through this damaged mucosa and caused the focal liver necroses and fatal terminal intoxication. This gives some evidence which may be interpreted to mean a definite but delayed injury of the mucous membrane of the intestine due to the roentgen rays. Some observers may wish to explain this apparent injury to the intestinal mucosa as being purely mechanical and the direct result of the violent diarrhea and vomiting of the preceding days. It is known that vigorous purgation in some animals may be associated with the appearance of intestinal bacteria in the blood stream.

TABLE V.—18–3—ROENTGEN RAY, SUBLETHAL DOSE, SLIGHT CLINICAL REACTION.

Date.	Weight, pounds.	Urine, c.c.	Nitrogen, grams.	Diet.	Remarks.
Nov. 14	37.25	520	3.25	400 c.c. water 100 gm. sugar	Dog normal.
15	36.50	460	2.69	"	
16	35.75	537	2.94	600 c.c. water 100 gm. sugar	
16	Roentgen ray—200 ma. min., 2 mm. aluminum filter, spark gap 9 inches.				
17	35.31	671	3.86	400 c.c. water 100 gm. sugar	Dog normal.
18	35.43	550	3.47	"	Dog normal.
19	35.00	486	3.11	"	Given some food in error.*
20	34.37	955	4.76*	"	
21	33.75	480	2.94	"	Little vomitus.
22	33.19	509	3.39	"	
23	32.5	525	3.81	"	
24	32.06	596	4.20	....	Dog perfectly normal.

Autopsy (Dog 18–71, Table IV). Heart, lungs and thorax normal. Spleen less than two-thirds normal size and fibrous. Pancreas and adrenals normal. Kidneys specked with tiny red dots. Cortex is pale and architecture normal. Liver specked with orange-yellow dots and ecchymoses. Portal tissue is swollen and conspicuous. Stomach normal. Duodenum and jejunum show slight congestion. Ileum and colon present more marked congestion of the mucous membrane and some ecchomoses in the colon.

Microscopic Sections. Liver shows scattered focal hyaline necroses which involve parts of lobules and are not more than two days of age. Kidneys show little epithelial degeneration in the convoluted tubules. Pancreas and stomach normal. Ileum shows

slight edema of villi in places and increase in polymorphonuclear leukocytes. Evidently, in this case, there was an invasion of the blood stream by bacteria from the intestine during the last two or three days of life. This seems to be the best explanation of the liver necrosis and inflammatory reaction in the intestinal villi. Whether this reaction was primarily due to mechanical or roentgen-ray injury of the intestinal epithelium is open to debate.

Table V presents the data of an experiment with a sublethal dose of the roentgen rays. This dose of 200 ma. minutes may be considered as very close to the minimum lethal dose. This was a very active and strong dog, which may explain some of the individual tolerance. The increase in urinary nitrogen is definite for three days, but not extreme, and the clinical reaction is practically negative. Yet we can be sure from other experiments that a slight increase in the dosage would have precipitated a fatal reaction.

TABLE VI.—DOG 17-165—NEGATIVE ROENTGEN-RAY ANAPHYLAXIS.

Date.	Weight, pounds.	Urine, c.c.	Nitrogen, grams.	Diet.	Remarks.
April 14	23.63	337	2.66	400 c.c. water	Dog normal.
15	23.13	441	2.72	400 "	
16	22.88	414	2.69	...	500 c.c. glucose solution; 10 per cent. intravenously.
17	22.19	691	2.24	400 c.c. water	
18	21.94	339	2.77	...	500 c.c. glucose solution; 10 per cent. intravenously.
19	21.69	504	2.18	400 c.c. water	
20	21.50	712	2.02	400 "	
20	Roentgen ray—360 ma. min., 2 mm. aluminum filter, spark gap 6 inches.				
21	21.06	408	3.14	400 c.c. water	No clinical symptoms.
22	20.75	422	3.14	400 "	Normal.
23	20.38	473	2.58	400 "	
24	20.25	372	2.55	400 "	
25	20.06	397	2.49	400 "	
26	19.88	378	2.35	400 "	
			Second	observation.	
May 10	22.69	438	2.02	400 c.c. water	Dog normal.
11	22.31	407	1.74	400 "	
11	Roentgen ray—300 ma. min., 2 mm. aluminum filter, spark gap 6 inches.				
12	21.69	512	2.74	400 c.c. water	No clinical symptoms.
13	21.38	366	2.86	400 "	Dog normal.
14	21.06	452	2.10		
15	20.69	436	2.21	400 c.c. water	
16	20.56	385	2.02	400 "	
17	20.25	407	2.07	400 "	Dog normal.

That roentgen-ray anaphylaxis does not exist in dogs is clearly shown in Tables VI, VII and VIII. Table VI confirms the data in Table V to show that a dose of roentgen rays equivalent to 75 per cent. of the lethal dose or more may not disturb the nitrogen elimination in any considerable degree. The slight rise in urinary nitrogen appears in the two days following the roentgen-ray exposure

in both the primary and secondary observation. There is no difference in the nitrogen curve in either case and no clinical reaction. The data relating to the glucose injections is included for the sake of comparison with an experiment above. (See Table III.)

Table VII gives confirmatory data for the preceding experiment. The first dose is accompanied by considerable vomiting and diarrhea, but no signs of severe intoxication and little increase in the urinary excretion of nitrogen. A part of the reaction may be explained by the possibility that the sugar solution was somewhat irritating to this animal. There can be little doubt that a major part of the clinical reaction was due to the roentgen rays. The second dose caused no clinical reaction and little increase in urinary nitrogen. This exposure was shorter than the first but sufficiently large to rule out any anaphylaxis or even summation of intoxication, as the two roentgen-ray doses together are much over a lethal dose.

TABLE VII.—DOG 17-157—NEGATIVE ROENTGEN-RAY ANAPHYLAXIS.

Date.	Weight, pounds.	Urine, c.c.	Nitrogen, grams.	Diet.	Remarks.
Mar. 6	17.44	411	1.90	75 gm. sugar 400 c.c. water	Fasting four days.
7	17.06	381	1.93	"	Dog normal.
8	16.75	376	1.76	"	
8	Roentgen ray—400 ma. min., 2 mm. aluminum filter, spark gap 6 inches.				
9	16.25	Lost	..	75 gm. sugar 400 c.c. water	
10	16.00	383*	1.62	"	45 c.c. vomitus; diarrhea.
11	15.50	455*	1.96	"	Vomitus in urine.
12	15.06	291*	2.30	"	210 c.c. vomitus; diarrhea.
13	14.88	624*	1.74	"	Vomitus.
14	14.88	206*	2.02	"	430 c.c. vomitus; diarrhea.
15	14.88	395	1.62	"	Solid feces.
16	14.50	351	1.43	"	
17	14.38	380	1.40	"	Clinical improvement.
			Second observation.		
April 28	16.94	..	..	400 c.c. water	Dog normal.
29	16.50	424	2.07	400 "	
30	16.19	331	1.96	400 "	
30	Roentgen ray—300 ma. min., 2 mm. aluminum filter, spark gap 6 inches.				
May 1	15.75	457	2.04	400 c.c. water	No clinical reaction.
2	15.50	287	2.13	400 "	
3	15.13	408	2.10	400 c.c. water	Normal.
4	14.88	438	1.93	400 "	
5	14.50	411	2.04	400 "	Little diarrhea and vomitus.
6	14.31	401	1.82	400 "	
7	14.06	393	1.96	400 "	Dog normal.

* Vomitus and urine combined for N analysis

The experiment outlined in Table VIII is somewhat different in character, but the evidence against the roentgen-ray anaphylaxis is just as convincing. The first dose is relatively small (three-fifths of lethal with six-inch spark gap) and is followed by only a very

slight rise in the curve of nitrogen excretion, lasting three or four days. The second dose was practically twice a lethal dose, given by mistake, as the nine-inch spark gap was not taken into the calculation. In spite of the large dose and the preceding roentgen-ray exposure, the dog showed the usual latent period of two days during which there were no clinical symptoms. Death as usual followed on the fourth day, with the usual autopsy findings described above.

TABLE VIII.—DOG 18–36—NEGATIVE ROENTGEN-RAY ANAPHYLAXIS, SECOND DOSE LETHAL.

Date.	Weight, pounds.	Urine, c.c.	Nitrogen, grams.	Diet.	Remarks.
Sept. 15	24.00	395	2.30	400 c.c. water	Dog normal.
16	23.63	355	2.35	400 "	
17	23.00	370	2.49	400 "	
18	22.94	365	2.55	400 "	
19	22.63	437	2.24	400 "	
20	22.38	369	2.16	400 "	
20	Roentgen ray—300 ma. min., 2 mm. aluminum filter, spark gap 6 inches.				
21	22.00	445	2.35	400 c.c. water	
22	21.63	432	2.86	400 "	
23	21.31	410	2.58	400 "	
24	21.06	196	2.38	400 "	
25	20.81	385	2.11	400 "	
26	20.50	393	2.13	400 "	
27	20.06	382	2.04	400 "	
28	19.88	378	1.99	400 "	
29	19.44	366	2.02	400 "	Normal.
			Second observation		
Oct. 13	21.63	475	1.91	400 c.c. water	Dog normal.
14	21.25	368	1.82	400 "	
15	21.06	387	2.04	400 "	
15	Roentgen ray—400 ma. min., 2 mm. aluminum filter, spark gap 9 inches.				
16	20.25	575	3.19	400 c.c. water	Dog normal; no vomitus.
17	19.81	375	2.88	400 "	Dog normal; no vomitus.
18	19.13	598	3.64	400 "	Vomitus; dog not very sick.
19	Dead	575	2.02	....	Much bloody diarrhea in cage.

Autopsy (Dog 18–36, Table VIII). Heart, lungs and thorax normal. Spleen small and hard. Liver deep red and congested. Pancreas normal. Kidneys much congested; architecture normal. Stomach full of thin straw-colored fluid and mucosa normal. Duodenal mucosa deep red, congested and bile-stained. Jejunum and ileum show decreasing congestion of mucosa as the ileocecal region is reached. Colon shows red longitudinal ridges in its mucosa, and it is tightly contracted. Capillary engorgement of the viscera and intestinal tract is the only noteworthy abnormality.

Microscopic Sections. The intestinal mucosa in places shows definite hemorrhages and some epithelial degeneration, although complicated by postmortem degeneration.

The absence of any constitutional reaction associated with the

roentgen-ray burn is clear from the data included in Tables IX and X. Table IX shows a long latent period following the roentgen-ray exposure and the dermatitis which later developed into an ulcer or "burn." During the latent period there is no evidence of any increase in protein breakdown, and the nitrogen excretion is constant. When the skin is broken and moist following the dermatitis we note a slight rise in urinary nitrogen, which is due to the inflammatory reaction in the skin.

TABLE IX.—17–209—ROENTGEN-RAY BURN, NITROGEN METABOLISM UNDISTURBED.

Date.	Weight, pounds.	Urine, c.c.	Nitrogen, grams.	Diet.	Remarks.
Sept. 19	23.00	369	2.24	400 c.c. water	Dog normal.
20	23.25	418	2.16	400 "	
20	Roentgen ray—100 ma. min., no filter, spark gap 6 inches, left chest.				
21	22.81	426	2.24	400 c.c. water	Dog normal.
22	22.44	384	2.19	400 "	
23	22.0	410	2.13	400 "	
24	21.81	418	2.04	400 "	
25	21.25	431	1.71	400 "	
26	21.06	399	2.02	400 "	
27	20.56	393	1.88	400 "	
28	20.38	414	2.07	400 "	
29	20.19	369	1.90	400 "	
30	..	..	2.04	400 "	
Oct. 1	19.50	456	1.71	400 "	Skin is normal.
2	19.13	446	1.57	100 gm. sugar 400 c.c. water	
3	19.25	358	1.29	"	
4	19.13	307	1.04	"	
5	19.06	356	1.57	"	Slight dermatitis and loss of hair.
6	19.06	375	1.12	"	
7	18.94	387	1.23	"	
8	18.75	407	1.23	"	
9	18.63	406	1.23	"	
10	18.50	424	1.29	"	Skin moist and tender.
11	18.25	417	1.31	"	
12	18.13	414	1.26	"	
13	17.94	382	1.34	Mixed diet	Dog active and lively; roentgen-ray burn is moist and somewhat tender.
17	19.19	Sacrifice		"	

Autopsy (Dog 17–209, Table IX). The organs are normal.

Microscopic Sections. Microscopic sections add nothing of importance. There is little reaction in the superficial skin lesion due to the roentgen rays.

The data in Table X is not quite so satisfactory as that given above (Table IX), but in general confirm the preceding experiment. There are periods of slight increase in urinary nitrogen after both roentgen-ray exposures, but there was clinical evidence of a very slight distemper which can modify the nitrogen elimination. The

latent period here was about three weeks between exposure to the roentgen rays and development of the "burn" or ulcer.

TABLE X.—17-134 (1)—ROENTGEN-RAY BURN, DELAY IN REACTION.

Date.	Weight, pounds.	Urine, c.c.	Nitrogen, grams.	Diet.	Remarks.
Feb. 17	15.75	211	1.26	100 gm. sugar, 400 c.c. water	Dog normal.
18	15.50	327	1.29	"	
19	15.44	331	1.09	"	
20	15.25	313	1.12	"	
20	Roentgen ray—500 ma. min., no filter, spark gap 6 in., left hind quarter.				
21	15.25	303	1.18	100 gm. sugar, 400 c.c. water	No clinical symptoms.
22	15.06	400	1.23	"	
23	15.00	297	1.12	"	
24	14.94	336	1.29	"	
25	14.81	321	1.18	"	
26	14.69	346	1.40	"	
27	14.56	328	1.23	"	
28	14.38	353	1.29	"	
Mar. 1	14.00	393	1.23	"	
1	Roentgen ray—800 ma. min., no filter, spark gap 6 in., right hind quarter.				
2	13.75	368	1.29	100 gm. sugar, 400 c.c. water	
3	13.25	548	1.57	"	
4	..	386	1.68	"	
5	12.69	468	1.62	"	
6	12.50	450	1.51	"	Evidences of very slight distemper.
7	12.38	447	1.51	"	
8	12.25	460	1.34	"	
9	12.19				
10	12.69	133	1.34	"	
11	12.63	347	1.15	"	Skin everywhere normal.
17	Dermatitis left leg.				
20	Early ulcer right leg.				Dog active and eats well.

The question of tolerance to the roentgen rays is raised by the experimental data of Tables X and XI. This dog was exposed to the unfiltered roentgen rays on two occasions to produce a burn or roentgen-ray ulcers. Three months later the dog was given a supposedly lethal dose (500 ma. minutes, six-inch spark gap). For a dog of this size the dose was considered surely lethal. The dog was very sick and showed all signs of a very severe intoxication—vomiting, diarrhea, prostration, leukopenia and some increase in blood non-protein nitrogen. The severest symptoms appeared on the fourth day, and after this there was slow improvement to complete recovery. The urinary nitrogen shows much increase, especially on the fourth and fifth days, when it was over twice normal. We may say that this dog had developed a very slight tolerance to the general roentgen-ray intoxication following the two previous exposures, or that this dog presented an abnormally high individual resistance to the intoxication.

TABLE XI.—17–134 (2)—ROENTGEN-RAY INTOXICATION, TOLERANCE (?) TO LETHAL DOSE.

Date.	Weight, pounds.	Urine, c.c.	Nitrogen, grams.	Diet.	Remarks.
May 29	15.56	340	1.96	400 c.c. water	Both legs show roentgen-ray ulcers. (See Table X.)
30	15.13	395	2.26	400 "	Dog active.
31	14.94	338	2.24	400 "	
31	Roentgen ray—500 ma. min., 2 mm. aluminum filter, spark gap 6 inches.				
June 1	14.50	391	2.80	400 c.c. water	White blood cells, 17,000.
2	14.13	417*	2.86	400 "	Vomitus.
3	13.56	641*	3.70	520 "	Vomitus; diarrhea.
4	12.75	632*	5.60	400 "	Dog very sick; white blood corpuscles, 2700; vomitus; diarrhea; blood N. P. N., 47 mg.
5	12.50	350	4.48	225 "	Vomitus and diarrhea.
6	12.56	187	5.26	400 "	Diarrhea.
7	12.06	385	3.30	400 "	Dog better.
8	12.06	75	2.41	....	Dog will recover.
8	Sacrifice. Blood N. P. N., 29 mg.				

* Urine contained vomitus.

(Dog 17–134 (2), Table XI). This dog was exposed to the roentgen rays on February 20 (50 ma. minutes) and March 1 (80 ma. minutes). Spark gap six inches; no filter in each instance. Dermatitis appeared over the first area on March 17 and over the second area on March 20. Ulcers slowly developed, which tended to heal slowly in the following weeks. The dog was in excellent health, with good appetite and general activity.

June 8. Sacrifice by ether and bleeding. *Autopsy* at once. The organs of this dog were washed free from blood by the use of normal saline and various catalase determinations done. There seemed to be no striking abnormalities in gross.

Microscopic sections add nothing of importance.

TABLE XII.—DOG 18–72—CHLOROFORM AND ROENTGEN-RAY INTOXICATION.

Date.	Weight, pounds.	Urine, c.c.	Nitrogen, grams.	Diet.	Remarks.
Dec. 4	18.13	480	2.63	400 c.c. water	Dog normal.
5	17.56	398	2.88	400 "	
6	17.25	437	2.46	400 "	
6	Chloroform anesthesia, 1 hour.				
7	16.13	165	4.70	400 c.c. water	Dog not intoxicated.
7	Roentgen ray—200 ma. min., 2 mm. aluminum filter, spark gap 9 inches.				
8	15.75	345	5.32	400 c.c. water	Dog is much intoxicated.
9	15.56	325	4.59	300 "	Vomitus and diarrhea.
10	15.19	381	3.42	110 "	Dog is sick.
11	14.56	195	3.36	200 "	Diarrhea marked.
12	14.50	152	2.97	200 "	
13	14.13	277	2.94	200 "	Clinical improvement.
14	13.81	237	2.97	200 "	
15	13.56	220	2.69	200 "	Dog no longer intoxicated.
16	13.31	305	2.80	200 "	Ether and sacrifice.
16	Blood non-protein nitrogen, 36 mg., and urea N, 26 mg. per 100 c.c.				

Tables XII, XIII and XIV may be considered together. They show convincingly that chloroform poisoning and liver necrosis do not modify the general constitutional reaction to the roentgen rays whether a sublethal or lethal dose be given. Table XII gives the data to show very beautifully the summation in urinary nitrogen elimination, due in part to the chloroform injury and in part to the severe roentgen-ray intoxication. The nitrogen curve does not fall to normal even within ten days and autopsy shows the incomplete repair of the liver necrosis. The roentgen-ray exposure in this experiment (200 ma. minutes, nine-inch spark gap) is very close to the lethal dose; in fact, this may be a lethal dose to some dogs. The clinical reaction is certainly due to the roentgen-ray intoxication and not to the chloroform injury, which is not sufficient in itself to give rise to clinical symptoms.

Tables XIII and XIV show a lethal dose of roentgen ray superposed on a chloroform injury. The chloroform injury in Table XIII was slight because of the sugar feeding, but was moderately severe in Table XIV, a fasting experiment. The chloroform injury was scarcely sufficient to account for any of the clinical symptoms except the icterus (Table XIV). The largest dose of roentgen rays (Table XIV) was responsible for a very clean-cut injury of the epithelium in the intestinal mucous membrane. It is reasonably certain that this injury is due to the roentgen rays and is responsible for the rapid postmortem autolysis of the intestinal epithelium which was described in the preceding experiments. (See Table XIII and I.) This whole picture makes it very unlikely that the roentgen rays have any specific injurious effect on the epithelium of the liver, for the general reaction is not modified in the slightest by the presence of a definite degree of liver necrosis.

TABLE XIII.—DOG 18–33—CHLOROFORM AND ROENTGEN-RAY INTOXICATION.

Date.	Weight, pounds.	Urine, c.c.	Nitrogen, grams.	Diet.	Remarks.
Oct. 21	21.63	470	2.24	400 c.c. water	
22	21.31	420	2.16	400 "	Diarrhea.
23	21.00	452	2.18	75 gm. sugar 700 c.c. water	Blood N. P. N., 37 mg.
24	20.94	620	2.44	75 gm. sugar 300 c.c. water	
25	20.56	438	1.62	"	
25	Chloroform anesthesia, 1 hour.				Diarrhea.
26	19.81	452	2.49	75 gm. sugar 300 c.c. water	Diarrhea.
27	19.31	455	4.62	"	
27	Roentgen-ray, 300 ma. min., 2 mm. aluminum filter, spark gap 9 inches.				
28	19.06	372	4.93	75 gm. sugar 300 c.c. water	Diarrhea; dog sick.
29	18.75	653	5.10	"	Vomitus; dog sick; blood N. P. N., 41 mg.
30	18.06	507	4.93	"	Vomitus and diarrhea; blood N. P. N., 52 mg.
31	Dead	965	3.89	....	Bloody vomitus; diarrhea.

Autopsy (Dog 18–72, Table XII). Heart, lungs and thorax normal. Spleen tough and fibrous, about two-thirds normal size. Pancreas, adrenals and kidneys normal. Stomach and intestinal tract normal. Liver below normal in size, tough and fibrous. Lobules show depressed centers, which are red. The mid-zone of each lobule is yellowish and contains fat. The peripheral or portal zone is gray and translucent. Gall-bladder is distended.

Microscopic Sections. Liver shows incomplete repair of the chloroform injury, which probably involved about one-third to one-half of each lobule. Spleen, kidney and intestine negative.

Autopsy (Dog 18–33, Table XIII). Heart, lungs and thorax normal. Spleen thin and hard. Pancreas normal. Liver dark red and congested. Section is gelatinous and translucent. No evidence of chloroform necrosis. Kidneys normal except congestion. Stomach and intestinal tract show a little postmortem change, but definite congestion of the mucous membranes is most marked in the duodenum and jejunum. No ulcers and no definite hemorrhages.

Microscopic Sections. Spleen and pancreas are normal. Kidney shows cloudy swelling of the convoluted tubules. Liver is normal. The sugar evidently protected the liver against the chloroform injury or the repair of the injury was complete. Stomach normal. Small intestine shows much autolysis of the epithelium in the crypts as described above. (Dog 18–45, Table I, Autopsy.) There is an increase in polymorphonuclear leukocytes in the stroma of the mucous membrane, which indicates a definite antemortem injury done to structures in this mucosa.

TABLE XIV.—DOG 18–46—CHLOROFORM AND ROENTGEN-RAY INTOXICATION.

Date.	Weight, pounds.	Urine, c.c.	Nitrogen, grams.	Diet.	Remarks.
Oct. 2	25.63	461	2.13	400 c.c. water	
3	25.13	466	2.21	400 "	Blood N. P. N., 35 mg.
4	24.44	371	2.44	400 "	Diarrhea.
4	Chloroform anesthesia, 1 hour.				
5	23.88	432	3.53	400 c.c. water	No clinical intoxication.
5	Roentgen ray, 400 ma. min., 2 mm. aluminum filter, spark gap 9 inches.				
6	23.38	545	4.65	400 c.c. water	Dog is dull.
7	22.38	630	7.79	400 "	Dog is dull.
8	21.31	445	9.25	400 "	Vomitus; bloody diarrhea; icterus; dog very sick.
9	21.06	506	7.18	....	Dog very sick; sacrificed.
	Dog would die in a few hours; blood N. P. N., 100 mg.				

Autopsy (Dog 18–46, Table XIV). Icterus marked. Blood clots in normal time and clots are rather soft. No ecchymoses in tissues. Heart, lungs and thorax normal. Spleen small and fibrous. Kidneys and pancreas normal. Mesenteric glands deep red and moist. Liver very yellow and fatty. Lobulation uniform, with red centers,

fatty mid-zone and translucent marginal or portal zone. Stomach contains blood-tinged fluid. Mocosa slightly swollen and deep pink color. Duodenum shows a deep pink mucosa and contains much blood-tinged fluid. Very little mucus. Small intestines are moderately contracted. There is definite congestion of the mucous membrane, but little mucus secretion. Colon shows the same congestion and contains thin blood-tinged feces.

Microscopic Sections. Spleen, kidney and adrenals negative. Liver shows hyaline necrosis involving about one-half of each lobule. There has been practically no repair of this injury, which usually proceeds so rapidly. This is due in part to fasting and in part to the roentgen-ray treatment. Small intestines in many places show definite injury of the epithelium lining the crypts and accumulation in such areas of clusters of polymorphonuclear leukocytes. There is little if any edema of the interstitial tissue, but some increase in polymorphonuclear leukocytes. Colon shows great increase in mucous accumulation in its crypts and some epithelial injury and groups of polymorphonuclear leukocytes.

TABLE XV.—SUMMARY OF ROENTGEN-RAY INTOXICATION EXPERIMENTS.

Experiment No.	Roentgen ray.		Delay in clinical reaction (days).	Blood.		Death after roentgen-ray exposure (days).	Remarks.
	Milliampère min.	Spark gap, inches.		Non-protein nitrogen, mg. per 100 c.c.	Urea nitrogen, mg. per 100 c.c.		
18–45	500	9	1.0	50*	..	3.5	
18–69	220	9	2.5	59	24	4.0	
18–71	210	9	2.0	..	..	9.5	
18–52	380	9	1.0	47*	..	3.5	
18–55	300	9	2.0	58*	..	3.5	
18–61	300	9	2.0	78	49	4.0	
17–10	500	6	0.5	168	102	3.0	
17–172	500	6	1.5	201	..	7.0	
16–110	500	6	0.5	172	94	7.0	Renal calculus.
17–134	500	6	1.0	29	..	Recovery	Tolerance (?).
18–72	200	9	..	36	26	Sacrifice	Chloroform added.
18–46	400	9	..	100	59	4.0	Chloroform added.
18–33	300	9	..	52*	..	3.5	Chloroform added.
18–36	300	6	Neg.	..	..	..	No intoxication.
18–36	400	9	2.5	40*	..	3.5	Second exposure.
17–157	400	6	1.0	..	..	Recovery	Severe intoxication.
17–157	300	6	Neg.	..	..	"	Second exposure.
17–165	360	6	Neg.	..	..	"	No intoxication.
17–165	300	6	Neg.	..	..	"	Second exposure.
18–43	160	9	2.5	..	..	"	Slight intoxication.
18–3	200	9	4.0	..	..	"	Slight intoxication.

* Blood obtained on day before death.

A summary of all the experimenta described above is given in Table XV. This table brings out many interesting points and emphasizes particularly the latent period, during which time the dog

appears to be perfectly normal—a latent period of twenty-four to forty-eight hours, as a rule. The clinical intoxication appears suddenly and runs a stormy course, usually resulting fatally on the fourth day. The blood non-protein and urea nitrogen are usually much increased above normal on the day before death or a few hours before death or sacrifice.

The most striking point about the roentgen-ray intoxication brought out in Table XV concerns the length of spark gap. It is very obvious that the rays from the nine-inch spark gap are very much more toxic than those from the six-inch spark gap. This is of considerable practical importance, and is not generally recognized.

Discussion.

Let us review in a few words the *clinical picture* of the general constitutional reaction following a suitable exposure of a dog to the filtered hard roentgen rays of the Coolidge tube. The striking latent period is almost always present and may last twelve to twenty-four hours, or even two days, during which time the dog is lively, active and normal to careful examination. There is an increase in urinary nitrogen excretion during this period, indicating that tissue injury and disintegration have already taken place. Gastro-intestinal symptoms are the conspicuous feature of these cases, vomiting and diarrhea becoming marked after the latent period and bearing no relation to food intake. There is usually complete loss of appetite, but water is taken eagerly. The intoxication and general depression may appear after twelve hours, but much more frequently after twenty-four to forty-eight hours. Prostration in fatal cases usually appears on the fourth day, when the initial intoxication reaches its peak and death usually occurs at this time. A few cases pass this period of severe intoxication, show improvement and after three to four days succumb, with recurrence of gastro-intestinal symptoms. In these cases we find evidence of secondary infection which may be relatively slight, but too great a burden for the severely intoxicated animal.

It is remarkable that the maximum intoxication appears so constantly on the fourth day after exposure to the roentgen rays. Even in the experiments in which death came on the seventh, eighth or ninth days there was a period of great clinical intoxication on the fourth day. When the fourth day is safely passed in such experiments we have a right to anticipate complete recovery, although the period of convalescence may be long and the increased nitrogen elimination last seven to ten days. The constancy of this maximum intoxication on the fourth day must have significance in any explanation of this general systemic roentgen-ray intoxication. It is noteworthy that this reaction is independent of size of dose, for death is to be expected on the fourth day whether a single lethal dose or twice a lethal dose be administered.

It is well established by reports of many workers that the general systemic reaction to the roentgen rays is associated with *increased nitrogen elimination* in the urine. This applies to human beings, rabbits, guinea-pigs, rats, mice, dogs, cats, etc. It is usually possible to demonstrate an increase in purin bases and phosphorus radicles in the urine, which indicate the disintegration of cell nuclei, but not necessarily only the nuclei of leukocytes, as some would have us believe. This increase in urinary nitrogen may not be a true index of the severe reaction which may cause fatal intoxication. It is well to recall the curve of nitrogen elimination associated with a sterile abscess (Cooke and Whipple[10]), in which experiment the nitrogen excretion may rise 100 to 200 per cent. or more above the base line. Such an increase dwarfs the considerable nitrogen excretion excess in the roentgen-ray experiments, which rarely show more than 50 to 75 per cent. rise above the base line. Evidently there is a very different type of protein breakdown in these two experiments.

Our experiments show a definite increase in the *non-protein nitrogen* of the blood. This rise is usually distinct on the day before death (even twice normal) and may reach a very high level on the day of death (even more than 100 mg. per 100 c.c. blood). It is clear there is an increased breakdown of body protein, but this alone may not explain the heaping up of nitrogenous split products in the blood, for there may be faulty elimination. It has been claimed by many that the roentgen-ray intoxication is associated with or even in part due to a roentgen-ray nephritis, but the evidence for a true nephritis will not bear careful scrutiny. Many careful workers report negative findings, and others at the most report a little injury of the tubular epithelium in some experimental animals. There is little or no evidence of any nephritis from a study of the urine. We can state that our animals gave no evidence of any nephritis due to the roentgen rays nor even any constant anatomical changes which we could recognize in the renal epithelium. However, this does not rule out an impairment of renal function as a possibility even in the absence of histological evidence. Some work done in this laboratory by Mr. McQuarrie will show that certain proteoses can injure the renal cells to such a degree that renal function may be depressed below one quarter of normal for many hours followed by slow recovery to normal. Even the finest histological technic and vital stains cannot give evidence of any anatomical injury to account for this remarkable impairment of function. We hope to study the roentgen-ray intoxication in a similar fashion and to report on these experiments in the near future.

Anatomical changes certainly are not conspicuous in animals dead from the constitutional roentgen-ray intoxication. The spleen is decreased in size, fibrous and contains fewer lymphocytes than normal. Bone-marrow shows a decrease in cells. The parenchymatous organs may be passed over as normal, as there are no

constant abnormalities in gross or under the microscope. The striking symptoms are gastro-intestinal, and the entire tract was examined with much care in all our experiments. The contents may be slightly blood-tinged or even quite dark in the colon, but there are no ulcers of any kind. The stomach usually is normal in gross and microscopically. The small intestine in fatal cases usually shows a mottled mucosa, with patches of congestion often more marked in the jejunum. These patches are very indefinite and shade off into the normal mucosa, but there is distinct engorgement of the capillaries and villi in such areas. The colon may show some patchy congestion and may be tightly contracted. The small intestine has a tendency toward spastic contraction. The *intestinal tract* shows certain abnormalities, concerning which we are not quite satisfied. More work is needed in this field, and we hope to get more data in the near future. Certain experiments in which large doses of the roentgen rays were given show slight but definite abnormalities in the intestinal mucosa. Some of the crypts show degenerated epithelium and large clumps of polymorphonuclear leukocytes grouped about this epithelium and in the mucosa close to the basement membrane of the crypt. The tips of the villi were not included in this reaction. Furthermore, certain experiments showed a most remarkable speed of *autolysis of the intestinal epithelium*. Dogs which were autopsied six to twelve hours postmortem, whose organs showed a minimum degree of postmortem change, presented remarkable histological sections of the intestinal mucosa. The intestinal epithelium had *completely* autolyzed and vanished, leaving only a few epithelial fragments. Such changes cannot be due to the ordinary postmortem changes observed in intestines, as these changes involve the surfaces first, especially the tips of the villi, and spare at first the depths of the crypts. We feel that these observations furnish evidence that these epithelial cells are injured in some way during life and that this injury may be in part responsible for the dominant gastro-intestinal symptoms. One might postulate a very unstable equilibrium of the ferment-antiferment balance due to roentgen-ray exposure, but the term *injury* is just as intelligible. It is admitted that cancer cells and spleen cells are injured by the roentgen rays, and after exposure many of these cells vanish by autolysis *in vivo*. Also, it is known that cancer cells and spleen cells *in vitro* will autolyze faster after exposure to the roentgen rays.

We know that disturbances of the intestinal epithelium react promptly with the production of intoxication—for example, volvulus, intussusception and obstruction. If there is a constant and definite injury of intestinal epithelium caused by the roentgen rays we have a good basis for the clinical intoxication and gastro-intestinal symptoms as well as a new lead by which to study the general disturbances of the intestinal mucous membrane.

Roentgen-ray anaphylaxis is a term which has appeared recently in the literature (Bergonie[4]) to indicate a greatly increased sensitiveness to the roentgen rays after a time interval of weeks following the first exposure. Our experiments prove there is no such anaphylaxis nor is there even any difference in the nitrogen excretion, which is a more delicate index for sublethal doses of the roentgen rays than are the clinical symptoms. Whether there may be a certain amount of "summation effect" of the roentgen rays we cannot say with certainty. It is probable that a second dose of the roentgen rays given before the first reaction had subsided would give a more profound reaction. This period of reaction and increased nitrogen elimination may last seven to ten days, and at times even longer, but we have no evidence that a second dose of the roentgen rays given *after* this reaction period may cause any summation effect, anaphylaxis or other unusual reaction. We have some evidence that a very low-grade *tolerance* may develop following repeated exposure to the roentgen rays, but the margin of safety is very low and may come within individual variation to the roentgen-ray treatment.

Chloroform necrosis of the liver was combined with roentgen-ray injury because of several interesting possibilities. It has been suggested that the roentgen rays act primarily upon ferments, and consequently upon the cells which are richest in cell ferments. It is known that the liver cells are very rich in ferments and it is very easy to cause a necrosis of one-half of each liver lobule by a suitable dose of chloroform. Some liver cells which escape necrosis are damaged, and possibly as a result are more susceptible to other agents which injure liver cells. Superimposing a maximal sublethal roentgen-ray dose upon a chloroform liver of this sort should give a modified reaction if the liver takes a prominent part in this reaction. (See Table XII.) The reaction is not modified by the presence of the chloroform necrosis of the liver, but the nitrogen elimination shows a very pretty summation of the chloroform injury plus the roentgen-ray reaction. This is strong evidence surely that the liver does not play any essential part in the constitutional reaction to the roentgen rays.

This general systemic reaction which may follow the use of the roentgen rays in therapeutic doses has another appeal to the investigator. This reaction must be "*non-specific*," as no group of bacteria can possibly be concerned. If any injurious substances are formed in the body these substances must be formed from body tissues or fluids and not from any protein substances introduced. It seems safe to assume that the body protein must be injured in some fashion, as there is a distinct increase in urinary nitrogen and in the non-protein nitrogen of the blood. In fact, the primary injury may react upon the body protein in some manner so that the tissue autolysis of the injured protoplasm may form toxic split products which cause further injury to the body protein—a vicious circle.

The intoxication associated with an acute hemorrhagic pancreatitis is a good example of this type of reaction when the primary injury is inflicted upon parenchyma cells rich in enzymes. It is easy to suppose an autolysis of this protein material by these intracellular enzymes and the formation of toxic split products which may cause even a rapidly fatal intoxication. There are many points in common when we review the picture of roentgen-ray intoxication and of acute pancreatitis.

Intestinal obstruction is another example of a "non-specific" intoxication in which there is a great breakdown of tissue protein, as indicated by the nitrogen elimination in the urine and the accumulation of non-protein nitrogen in the blood (Whipple, Cooke and Stearns[58]). The clinical picture of acute intestinal obstruction presents a remarkable parallel to the clinical story of the fatal roentgen-ray intoxication. Death may take place at about the same interval after the initial roentgen-ray injury or obstruction, violent gastro-intestinal disturbances dominate the picture in both conditions and there is every evidence of great tissue injury and increased tissue katabolism. There is evidence for a perverted secretion (obstruction) or actual injury (roentgen rays) of the intestinal epithelium in these two conditions.

The *sparing action of carbohydrates* is illustrated in Tables III and VI. The glucose solutions are given intravenously during the most acute stage of intoxication (Table III) and cause a remarkable retention of nitrogen as appearing in the next day's urine. Compare with this the reaction in the normal dog (Table VI). More work is to be done to explain this peculiar retention of nitrogen, and we do not wish at this time to advance any explanation. It is to be observed there was some clinical improvement, and this suggests glucose solutions intravenously as proper treatment for severe cases of general intoxication from the roentgen rays.

The *destruction of leukocytes* by the roentgen rays is well known and serves as the best example of the specific susceptibility to the roentgen rays which is exhibited by certain body cells—for example, leukocytes, germinal cells and cancer cells. Earlier workers who recognized the destruction of the leukocytes tried to explain the general intoxication as a result of the leukotoxin or leukoferments which were set free in the blood. One cannot deny that such products resulting from destruction of the leukocytes may be toxic, but the evidence is against this, and it remains for the proponents of this hypothesis to bring some direct evidence. We know that it is possible to destroy leukocytes in enormous number in the circulation by the introduction of certain organ extracts, yet these reactions can scarcely be said to parallel the intoxication resulting from roentgen-ray exposure. It is possible to destroy great numbers of leukocytes in animals in health or in human beings in disease (leukemia) by small doses of the roentgen rays without any signs of

intoxication. The difficult thing to explain is the peculiar *latent period* of the roentgen-ray intoxication.

The *roentgen-ray burn* again offers the obstacle of the *latent period*. There may be a period of three weeks between the roentgen-ray exposure and the subsequent dermatitis, with loss of epithelium and ulcer formation. One may fall back on the sluggish metabolism and slow growth of the epidermis, yet on occasions the growth of this epithelium may be quite rapid (healing of wounds). The solution of this riddle is not yet at hand.

The *spark gap* is to be emphasized from a study of our fatal cases. As the spark gap is increased the voltage of the electric current is raised and the hardness or penetrability of the rays is increased. The fatal dose for a dog is about 500 ma. minutes with a six-inch spark gap, but only 210 ma. minutes with a nine-inch spark gap. We believe that this fact is not clearly recognized by roentgenologists, and it should be repeatedly emphasized.

It should be noted that the experiments with the six-inch spark gap were performed with an old machine with rheostat control. The nine-inch spark gap experiments were performed with a new and more powerful machine having an autotransformer control. In other experiments we expect soon to control these variables and ascertain the actual voltages which may be a more accurate measure for the toxicity of the roentgen rays than is the spark gap.

Catalase is a ferment which has been studied by many workers and recently by Burge,[6] who attempts to explain and correlate a variety of life processes with fluctuations in the catalase content of organs. We are not able to follow him in many of his explanations, but it seemed worth while to contrast the catalase content of normal and rayed tissues. A large number of analyses were determined by the usual methods and extracts made in a variety of ways from normal and rayed organs. Many observations were made upon animals which had been exposed to a lethal dose of the roentgen rays. At the death or after sacrifice the organ extracts were made, some after washing the organs free from blood and others containing blood. These analyses were compared with controls done in the same way omitting the roentgen-ray exposure. Animals were fasting and all conditions were uniform. Variations in figures were as great in the controls as in the rayed animals, and we feel that if the catalase determinations have any value they indicate that this ferment is not disturbed by the roentgen rays. In our hands the individual fluctuations in normal animals are so great as to arouse suspicion in our minds as to minor fluctuations under experimental conditions. We feel that all catalase work must be controlled by a large number of check experiments before a proper interpretation of experimental changes can be reached. So far as we are aware, Burge has published very few control experiments in his many papers.

The question of *ferments* and roentgen-ray exposure is a most

important one. When we finish the analysis of the anatomical changes caused by the roentgen rays and the review of the clinical symptoms of intoxication which may be due to the specific action of the roentgen rays on the leukocyte or the intestinal epithelium or the epidermis, we come up against the fundamental question: How do the roentgen rays injure a living cell? It is claimed by Hertwig[23] that the chromatin is first injured and that this injury is the fundamental one. But Richards has shown that the cytoplasm is also injured. Many workers are tempted to leave the morphology of the cell and venture into the field of cellular ferments which is equally difficult, to say the least. One must be very careful in accepting *in vitro* ferment experiments on unicellular organisms or isolated ferments to explain ferment reactions in the living complex of a warm-blooded animal.

Yet there are observations which indicate that the body ferments in the living cells are actually influenced by the roentgen rays. A spleen removed from a rayed animal will show more rapid autolysis than a control (Heile[19]). The same is true for cancer tissue (Neuberg[40]). Our experiments indicate that the same holds for the epithelium of the intestinal mucous membrane exposed to the roentgen rays. Richards[45 46] who has done the best experiments upon the roentgen rays and ferments is able to show *in vitro* that small doses of the roentgen rays accelerate and larger doses inhibit certain ferment action. He does not believe, however, that this direct action of the roentgen rays on ferments is adequate to explain all the reactions of a living cell to the roentgen rays. This conservative opinion should have much weight.

We must not lose sight of the fact that the roentgen rays pick out certain cells with no apparent rhyme or reason. Why, for instance, is the leukocyte injured and the pancreatic cells, which surely are rich in ferments, escape entirely? Simple disturbance of cellular ferments by the roentgen rays cannot explain any such peculiar reaction as this just mentioned. There must be some initial stimulus or injury inflicted upon certain cells of the body and other body cells must be tolerant and escape this injury or stimulus. It is conceivable that the primary injury may form toxic split products which cause the final intoxication, but we have no right to assume this without some evidence, and this experimental evidence has not been submitted.

The word *injury* may be as good as any to indicate our belief that some change has been effected within the cell substance (nucleus or protoplasm). This change may influence, *first*, the cell protoplasm, cell lipoids, cell ferments, etc., but who is to say whether the structure or the ferment is first changed or "injured" by the roentgen ray? We know of many fundamental changes in cells, even fatal changes, which leave no trace that can be detected by modern histological methods. Yet we cannot accept such an instance with-

out question as an example of *primary* injury to the cell ferments. We are too apt to cloak our ignorance by the use of terms which have very little fundamental significance when subjected to analysis.

In the face of these difficulties the authors hesitate to outline the constitutional reaction to the roentgen rays as pictured in their minds and put forward this explanation with a proper regard for possible objections and criticisms. Exposure of a dog to the roentgen rays brings about certain changes (or "injury") in certain of the body cells. In some cells the injury may be evident in a short time (leukocytes) and in other cells the injury may be greatly delayed (epidermis). We cannot explain this latent period. It is at least possible that other body cells may be injured after a longer or shorter latent period depending upon the individual properties of the cells. The nitrogen elimination shows that the cell injury and autolysis begin promptly after exposure to the roentgen rays and continue with a rising curve to the fatal outcome. The blood non-protein nitrogen speaks for the same progressive destruction of body protein. We have evidence that the ferments in certain cells of the body are profoundly altered and take part in the cell destruction beyond a doubt, yet we cannot say that this ferment disturbance is not secondary to some "injury" of cell substance apart from the enzymes. There are individual peculiarities in the reaction of the cells to the roentgen rays which speak for an individuality in the cell reaction and this surely may not of necessity depend upon primary ferment change. The liver and pancreatic cells are rich in ferments yet so far as we know they escape the roentgen-ray injury. The epithelium of the small intestine is closely related to the liver and pancreatic epithelium yet it appears to be "injured" by the roentgen rays. Is this due to a primary injury of ferments? Then how may we explain the immunity of other parenchyma cells which contain similar autolytic ferments?

The obvious "injury" of the intestinal epithelium offers a satisfactory explanation for many of the clinical features of the fatal intoxication—vomiting, diarrhea and prostration. Disturbances of this epithelium can produce a severe intoxication (intestinal obstruction) and for this reason we think the injury of the intestinal epithelium by the roentgen rays plays no small part in the general systemic reaction and intoxication.

Summary.

The general constitutional reaction of dogs given a lethal dose of hard roentgen rays from the Coolidge tube is remarkably uniform and constant. A double lethal dose will not modify the clinical reaction. A latent period of twenty-four hours or longer is the rule and during this time the dog is normal except for an excreted urinary nitrogen. Vomiting and diarrhea then dominate the clinical picture until death which as a rule follows on the fourth day.

The blood non-protein nitrogen commonly shows a marked increase (twice normal) on the day before death and often more than three times normal on the day of death.

The elimination of urinary nitrogen is increased on the day following the roentgen-ray exposure and remains high until death, often an increase of 50 to 100 per cent. above the normal base line.

Autopsy findings are: a spleen which is small and fibrous, a moderate grade of congestion and mottling of the intestinal mucous membrane and strong evidence for *epithelial injury* in the intestinal mucosa. The epithelium lining the intestinal crypts may show actual necrosis and invasion of polymorphonuclear leukocytes. This epithelium also shows a remarkable speed of autolysis and may vanish by autodigestion within a few hours postmortem.

The epithelium of the small intestine apparently is sensitive to large doses of the roentgen rays, and the injury of these important cells may furnish the correct explanation of the general intoxication associated with the vomiting and diarrhea.

The so-called roentgen-ray anaphylaxis or hypersensitiveness to a second properly timed roentgen-ray exposure finds no support in our experiments. In fact, there is some evidence for a slightly increased tolerance to the second dose.

Chloroform injury and the associated liver necrosis do not modify the reaction of the dog to large or small doses of the roentgen rays. This is evidence that the liver epithelium is not fundamentally involved in the fatal roentgen-ray intoxication.

Our experiments yield no evidence of roentgen-ray nephritis.

Increasing the width of the spark gap increases the hardness or penetration of the roentgen rays, and this greatly increases the severity of the constitutional reaction and subsequent intoxication.

Burns caused by the roentgen rays are not associated with any distinct increase in urinary nitrogen during the long latent period between the roentgen-ray exposure and the early dermatitis which precedes the actual ulcer. We know of no satisfactory explanation for this long latent period, which may last for three weeks.

This roentgen-ray intoxication or general constitutional reaction is a good example of a "non-specific" intoxication. Much important information can be obtained by further study of this condition and will well repay the effort.

In conclusion, we wish to acknowledge with sincere appreciation the assistance of Dr. H. E. Ruggles, roentgenologist to the University of California Medical School and Hospitals, and the use of facilities placed at our disposal by the University Hospital.

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THE IMPORTANCE OF THE MOTION FIELD IN COMPARISON WITH THE FORM FIELD IN FAILING VISION.[1]

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George Riddoch,[2] from a study of records of cases of visual defects caused by injury of the occipital region of the cerebrum, makes certain important observations. He shows that:

Movement may be recognized as a special visual perception.

In restricted visual fields from occipital injuries in which some recovery of vision occurs, the first visual stimulus perceived, which can be recorded on a chart as a field, is movement. Therefore, appreciation of movement returns before the object, as such is recognized.

Recovery of vision for movement begins in the peripheral field.

Appreciation of movement and recognition of an object are always dissociated in patients in whom recovery of vision can be demonstrated; the field for the former, which is the more primitive perception, being the larger.

In prognosis this dissociation is a valuable aid, for when it is absent after a few months have elapsed no recovery of vision occurs.

He believes that the elementary visual perceptions of light, of movement, and of an object are dissociated in a manner similar to the dissociation which is known to occur when sensory paths conducting primary somatic sensory impressions of touch, of pain, of temperature are interrupted; by this I understand him to mean that probably distinct fibers are present in the visual system for the transmission of impressions of light, of motion, of form and of color. He mentions that it has long been known that the perceptions of light, of form and of color are to be found dissociated when the visual area is injured, and that it has also been recorded that coarse or even fine movements of the fingers may be detected before the fingers presented in the so-called blind field can be recognized. He states that hitherto the fields for movement have not been systematically charted nor has an attempt been made to inquire into visual dissociations in the light of recent additions to our knowledge of cerebral disturbances of somatic sensation. The whole subject has received greater interest since the investigations of Riddoch.

A patient has recently been referred to me by Major Charles H. Frazier with symptoms clearly permitting the diagnosis of tumor of the pituitary gland; acromegalic features, large feet and hands, etc. The roentgen-ray examination showed enlargement of the sella turcica. The patient, a woman, was admitted to the University

[1] Read before the Philadelphia Neurological Society, January 22, 1919.
[2] Brain, 1917, xl, 15.

Hospital, December 31, 1918. She had been under the care of Dr. Edward R. Evans, of Utica, N. Y., who reported that he had found decided choked disks. Each day as he tested for hemianopsia it seemed that objects in the left temporal field were considerably less distinct than in the right field. Vision steadily diminished during two weeks, and when examined by Captain Cross advanced optic atrophy was found in the left eye and much atrophy also in the right eye, with many fresh hemorrhages which probably accounted for sudden loss of vision.

In examining her roughly with the hand, with a black object 6 x 4 inches, or a white hairbrush, I found that with her left eye she saw movement only in the nasal field but could not tell what the object was. She had no vision in the temporal field even for motion. With her right eye alone she recognized a large object in both nasal and temporal fields, but more distinctly in the nasal field. She recognized movement promptly in both nasal and temporal fields of her right eye.

The examination on January 1, 1919, when the day was cloudy and electric light was used, showed that the patient was unable to detect an object at rest with her right eye, but could detect motion vaguely in both nasal and temporal fields of the right eye. At this time she could not detect motion in the nasal field of the left eye.

The examination on January 4, 1919 showed that in bright daylight with the left eye she could not distinguish light from darkness, once she saw a moving object in the nasal field and not at all in the temporal, but she could not see an object when still in either field of the left eye. With the right eye she could see objects still or moving in the nasal or temporal field.

The interesting feature of the visual examination was the ability to recognize movement in the nasal field of the left eye when the sight of the left eye was so far gone that the patient could not recognize form in the nasal field of the left eye and could not recognize either form or movement in the temporal field of the left eye. Even this limited vision was impaired within four days, and soon all vision in both eyes was lost. The recognition of movement only in the nasal field of the left eye conformed with the observation of Dr. Evans that vision first failed in the left temporal field, or at least failed more rapidly. My first examination was made at a time when all recognition of form had been lost in the nasal field of the left eye, while sufficient vision was still preserved here to permit the recognition of movement, and it probably could have been charted, and all other vision of this eye had disappeared. It would have permitted the conclusion, even if Dr. Evans's statement had not been obtained, that vision in the left eye probably failed first in the temporal field, and would indicate that the pressure came first on the inner fibers of the right optic tract or inner fibers of the left optic nerve. By discovering the recognition of motion in the nasal field

when all other vision in an eye seems to be lost, except perhaps that for light, we have a sign of value in suspected tumor of the pituitary gland. The sign may be of value when other signs of pituitary tumor are not conclusive.

The case to which I have just made reference shows that the field for motion exists independently of the other fields of form, light, color, in lesions of the optic tracts or chiasm as well as in lesions of the occipital lobe, but probably recognition of light is necessary for the proper recognition of motion. It shows that motion is probably the last form of vision to disappear, and is important in connection with Riddoch's statement that appreciation of movement returns before the object as such is recognized. His statement that light and movement are probably the most primitive of all visual percepts, and consequently they would be perceived first in a recovering blind field, explains also why motion is the last form of vision to disappear. Recognition of movement, as he says, is essential to animals both for hunting and for self-preservation; thus naturally it would have a wide field.

CONGENITAL DEXTROCARDIA.

By F. A. Willius, M.D.,
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Anomalies of the heart, partly because of their infrequent occurrence and partly because of their occult manifestations, are of particular interest to the clinician. I have recently been afforded the opportunity of observing three cases of congenital dextrocardia. Two types of this anomaly are recognized: one associated with transposition of the abdominal viscera (*situs transversus*), and the other, in which the transposition affects only the heart and great vessels. At times[3] anomalous arrangement of the venæ cavæ permits the admixture of arterial and venous blood; this gives rise to a clinical picture simulating the syndrome of congenital heart disease.

Recalling the embryological development of the heart, it is readily seen how transposition of this organ occurs. The two primitive cardiac tubes fuse into one about the fifteenth day[2] and an auricular, ventricular and bulbar subdivision becomes evident (Fig. 1). The tube soon becomes bent on itself, which determines largely the future axis of the heart. In congenital transposition the primitive tube bends into a contrasigmoid (S) instead of the normal sigmoid (S) manner. This has been explained[1] by assuming that the embryo lies in an abnormal position within the chorion, so that its right side instead of its left lies closer to the blood supply. The three

patients whom I examined presented the most frequent anomaly, dextrocardia with *situs transversus*. In no instance was there any complaint referable to the abnormality.

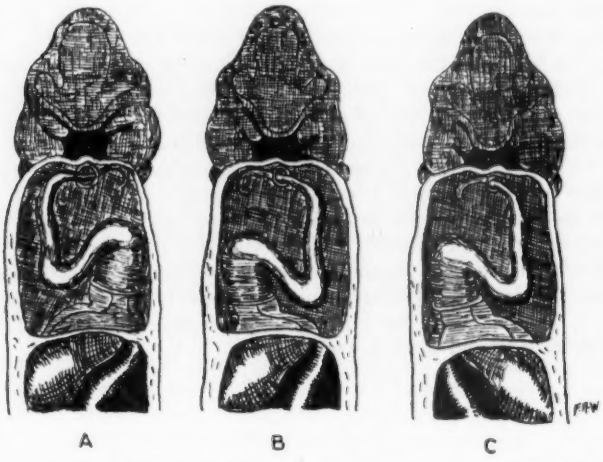


FIG. 1.—Transposition of the viscera in the embryo. *A*, normal; *B*, simple dextrocardia; *C*, complete situs transversus. Human embryo of about fifteen days. (After His.)

REPORT OF CASES.

CASE I (222329).—A woman, aged forty years, presented herself for examination complaining of chest pains of the intercostal

FIG. 2

neuralgic type. The apex-beat of the heart was palpable in the fifth right intercostal space 7.5 cm. from the midsternal line. The cardiac dulness extended 9.0 cm. to the right and 1.5 cm. to the left

of the midsternum. The heart sounds were best heard at the apex. Liver dulness was found to be on the left side and gastric tympany on the right. The systolic blood-pressure was 152, the diastolic was 90. Radiograms of the chest showed the dextrocardia and a trans-

FIG. 3

position of the stomach and colon (fluoroscopic colon). The electrocardiogram showed the heart-rate to be 94. Complete inversion of Leads I and II. The amplitude of the *R* waves in Leads I and II exceeded those in Lead III by one-third (Figs. 2, 3 and 4).

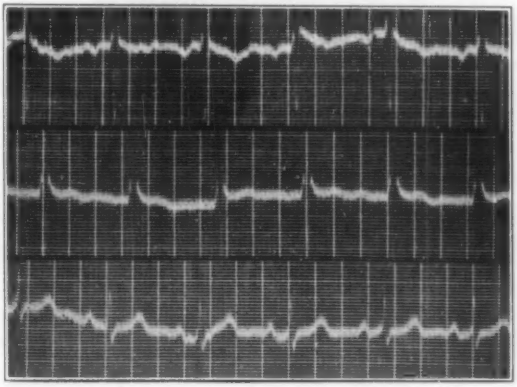


FIG. 4

CASE II (224506).—A woman, aged thirty-seven years, presented herself for examination on account of a pelvic complaint. The apex-beat of the heart was palpable in the sixth right intercostal space,

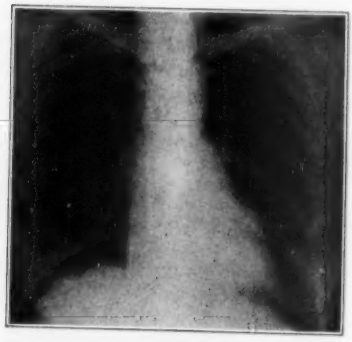


FIG. 5

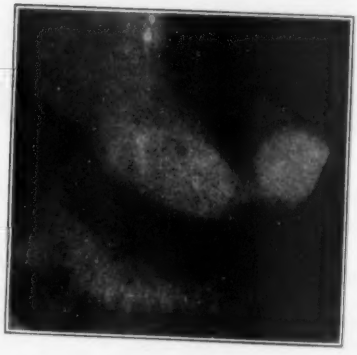


FIG. 6

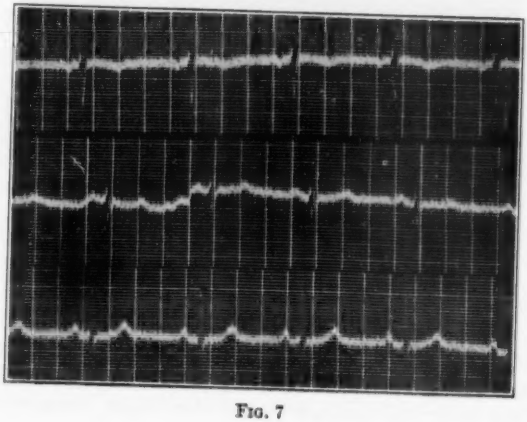


FIG. 7

9.0 cm. from the midsternal line. The cardiac dulness extended 11.0 cm. to the right of the midsternum. The heart sounds were best heard at the apex. Liver dulness was found on the left side and gastric tympany on the right. A bilateral salpingitis and a cyst of the left ovary were palpated. The systolic blood-pressure was 120, the diastolic was 75. The radiograms revealed dextrocardia and transposition of the stomach and colon (fluoroscopic colon). The electrocardiogram showed the heart-rate to be 75. There was complete inversion of Lead I. The amplitude of the *R* waves in Lead I were practically the same as those in Lead II and exceeded those in Lead III by slightly more than a third (Figs. 5, 6 and 7).

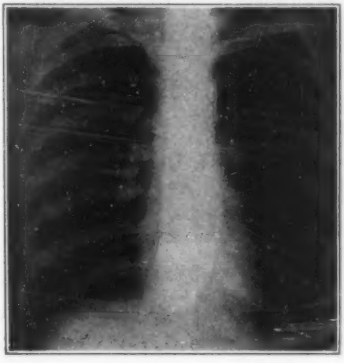


FIG. 8

CASE III (238633).—A woman, aged thirty-three years, presented herself for examination on account of goitre. The heart, as in the other cases, was found to be on the right side. The liver dulness was found on the left side and the gastric tympany on the right. The patient had a single adenoma of the right lobe of the thyroid 4.0 by 4.5 cm. The systolic blood-pressure was 112, the diastolic was 78. The radiogram revealed dextrocardia and transposition of the colon. The electrocardiogram showed the heart-rate to be 115; there was complete inversion of Lead I, and the amplitude of the *R* waves in Lead I were diminished to about one-half those of Lead III. The amplitude of the *R* waves in Lead III slightly exceeded those in Lead II. There was evidence of left ventricular preponderance (Figs. 8, 9 and 10).

The electrocardiograms of the last two cases essentially confirm the findings recorded in previous publications.[4 5 7 8] Lead I shows a complete inversion of all the deflections. Fig. 11 illustrates the angles produced by the direction of the leads and the resulting electrocardiograms. Case I (222329) shows the inversion also involving Lead II, and is explained by an exaggeration of the incli-

nation of the cardiac axis to the right. The leads represent fixed planes of electrical potential, and changes in cardiac position or alterations in muscle bulk preponderance obviously affect the electrical currents, as expressed by the electrocardiograms.

FIG. 9

It has been mentioned[6] that the *R* wave in Lead III becomes taller than in Lead II, but in these reported cases no constancy was

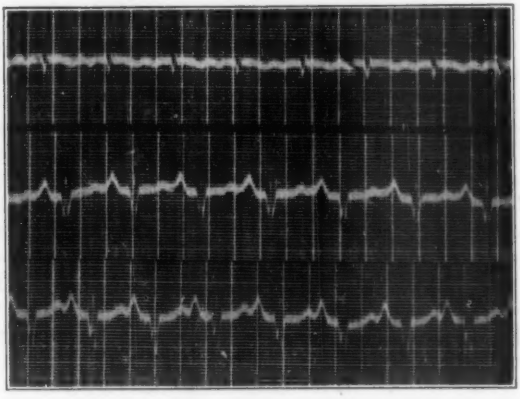
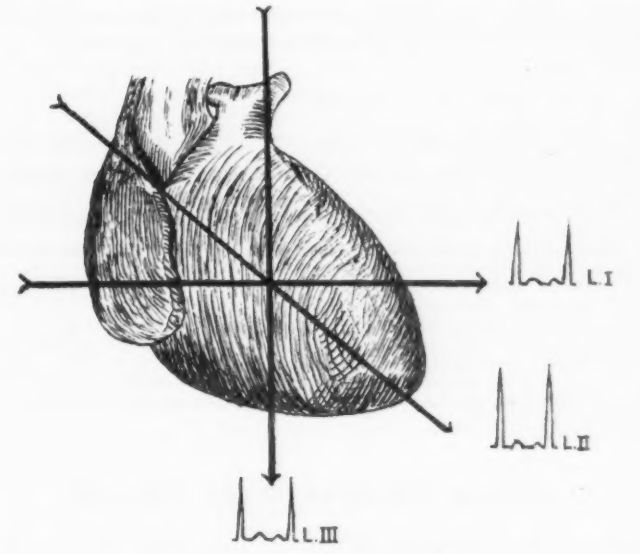


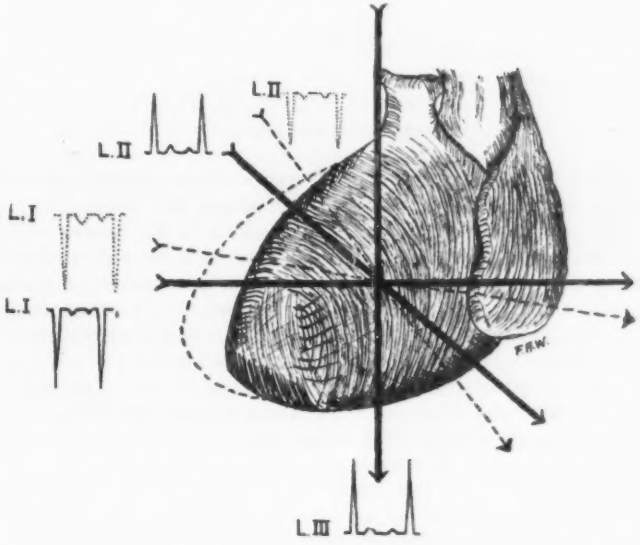
FIG. 10

observed. Hirschfelder mentions that the electrocardiographic curves sometimes are practically normal. Inversion of the deflections in Lead I is definite evidence of congenital dextrocardia with



A

Normal heart.



B

Congenital dextrocardia.

FIG. 11.—Schematic representations showing the angles produced by the direction of the leads and the resulting electrocardiograms. The dotted lines in Fig. *B* show the inclination to the right exaggerated and the inversion affecting Lead II.

situs transversus, and we recognize electrocardiography as a valuable adjunct in the differential diagnosis of cardiac displacements.

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PROTOZOAL INFECTIONS OF THE INTESTINES:

WITH EMPHASIS ON THEIR INCIDENCE AND BEHAVIOR IN OTHER THAN TROPICAL REGIONS AND ON THE PATHOGENICITY AND TREATMENT OF CERTAIN OF THE FLAGELLATES.

By Robert Pollock, M.D.,
and
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In war time the environment of every military camp is menaced by the diseases that become epidemic among the troops.

That protozoal infections are not confined to the tropics we are having abundant evidence from the reported cases and studies by men in every part of the country. These parasites are of special interest at present on account of the movement of carriers, due to war activities, with the infection of new regions and new contacts. In the Philippines and in the Canal Zone amebic dysentery was one of the foremost foes of white men, soldiers or civilians. Sanitation and preventive medicine are doing much to stop the spread of this and of other protozoal infections, but they must still be looked upon as dangers to camp life and to the adjacent communities.

This is particularly true now that we know of the existence of carriers who need never have visited in Southern countries and in whom the infection seldom declares itself in a frank dysentery, so that they go about for years improperly treated unless their physician is exceptionally thorough in his investigations.

The indications for fecal study were outlined by Sistrunk[1] in his paper, one of the early reports of so-called tropical infections occurring in residents of other regions. The stools of 110 patients with either chronic diarrhea, the passage of blood and mucus, anemia or obscure abdominal symptoms were examined. Of these, 65 had intestinal protozoa, chiefly amebas or trichomonas.

Smithies[2] reported in July, 1917, the study of the stools of 1000 patients at Augustana Hospital, in which series 98, or 9.8 per cent., showed intestinal protozoa either ameba or one of the flagellates. This report with others has undoubtedly quickened our interest in the subject and made us keener in searching for and recognizing the protozoa even though occurring far from the tropics. Practically all of Dr. Smithies' cases came from the northern half of the Central States. It is worthy of note that in most of his cases two or more varieties of protozoa were found in the stools.

It may not be out of place here briefly to summarize our knowledge of the habits of the parasitic protozoa and the principles governing their control.

Entamebic dysentery is caused by a distinct species of ameba (ameba histolytica), an obligatory parasite, whose host, so far as is known definitely, is man. The disease can reach the intestine of man only by the ingestion of material containing Entameba histolytica, generally in the encysted stage. These ameba may originate from acute cases or, more commonly, from convalescent carriers, or even from individuals who have never had dysentery, but are contact carriers. Such apparently healthy carriers on account of the cysts in their stools are more dangerous than the patient in the acute stage of the disease.

The flagellates (cercomonas, trichomonas, tetramitus) have not until recently been generally regarded as pathogenic. For this reason they have not been so thoroughly studied nor have means to combat them been so much searched for. In Panama the chief interest they called forth was the frequency with which they were associated with ameba, demanding more careful search for the latter. Trichomonas, the one most commonly found, does not form cysts so far as known, the so-called cysts being blastocystis hominis.

In regard to the flagellates, Brumpt[3] says that diarrheal conditions have been attributed to them when present in large numbers. A certain amount of irritation is necessary for their development, but once started, their multiplication may keep up a chronic intestinal catarrh. In the Andaman Islands, Anderson found trichomonas 723 times in 920 cases of dysentery, associated with ameba in 459 cases; flagellates were rare in 210 non-dysentery patients. Brumpt

[1] Jour. Am. Med. Assn., November 4, 1911, No. 19, lvii, 1507.
[2] Medicine and Surgery, July, 1917, p. 460.
[3] Parasitologie, Paris, 1913.

says that patients with monads almost always have a low or absent stomach acidity.

The attitude of the military surgeon to the protozoa is largely one of prophylaxis. Once having gained entrance to a camp, they tend rapidly to become epidemic and threaten to incapacitate large numbers of men. Such conditions call for the most intelligent and vigorous prophylactic measures, as shown by our experience in the Philippines, the Canal Zone and on the Mexican border.

The attitude of the civilian physician to the sporadic cases he meets is more one of the therapeutic handling of the individual case, although the protection of those about the patient ought not to be overlooked simply because it presents comparatively little difficulty.

The question of prophylaxis is essentially that in typhoid fever. The details of these prophylactic measures are so thoroughly standardized that we shall not enter into their discussion. As to the specific destruction of the intruder there is still much variation of opinion and the therapeutic treatment continues to tax the best efforts of clinicians. One after another, specific methods of treatment have been proclaimed as successful, only to give place later to a new method boasting a higher percentage of cures. Just what constitutes a permanent cure seems still a vexed question with certain authors. May not the difference in susceptibility of protozoa to chemicals, shown by Brem and Zeiler[4] in experimenting on ameba with quinin, and as suggested by them in reference to ipecac, determine to some extent the time demanded for permanent cure, as well as the selection of the chemical for the individual case?

A few facts related to treatment stand forth as apparently proved. Ipecac in some form seems to have a distinctly beneficial effect upon the symptoms and plays at least a part in practically all methods of treatment directed against the ameba, although upon the flagellates it seems to exert only temporary influence. It would seem that in the attack upon the ameba it is necessary to place the drug both in the blood stream and on the intestinal lining, although some clinicians (Manson, Dock, Niles and Simon) claim satisfactory results from the use of large doses of the powdered drug placed below the stomach by means of properly protected pills, a good description of which is given by Niles.[5] Others use the alkaloid emetin placed into the circulation by needle, sometimes supplemented by arsenic subcutaneously or intravenously. The advocates of both of these methods claim good results and see no need of colonic irrigations as an aid to the specific treatment.

It seems to be becoming more and more popular to attack every known or suspected protozoal infection, from pox to pellagra, by pumping arsenic into the circulation. We are, however, impressed with the results claimed by certain observers from the combined use

[4] Am. Jour. Med. Sc., November, 1910, p. 669.
[5] Ibid., October, 1914, p. 526.

of emetin hypodermically and salvarsan intravenously. The use of arsphenamin and neosarsphenamin has been extended to the amebic infections by Wynne,[6] and is now established as a definite treatment when used in connection with emetin. The recent paper by Dr. Herbert Gunn[7] at the meeting of the California State Medical Society is a valuable contribution to the treatment of carriers.

While touching briefly on treatment we cannot resist calling attention to the importance of detecting and subjecting to treatment the carriers of the Entameba histolytica. They are doubly dangerous in any community up to the time that suspicion is directed toward them, after which a careful study of the stool promptly identifies them, and they are then fair targets for therapeutic attack. These carriers present the ameba in the encysted form, which apparently is impervious to ordinary attack. An agent interesting to clinicians in this connection is the emetin-bismuth-iodide, which by some recent observers has seemed to be at least fairly satisfactory against encysted ameba. It is not claimed to have any appreciable effect upon flagellates. We feel also impelled to record the only method that with us has proved at all satisfactory in treating the flagellate trichomonas intestinalis, namely, the giving of large doses of calomel followed by saline purgation, once every four or five days, coupled with daily colonic irrigation of mercuric chloride (1 in 10,000 to 1 in 20,000). We are experimenting with other chemicals in the hope of finding something that will have a specific and permanent effect on them.

In a group of 46 cases coming under our notice during the past year, with symptoms seeming to demand a careful search for intestinal parasites, 19, or 41.3 per cent., showed protozoal parasites many times accompanied by other intruders. So frequently have the trichomonas presented, in association with troublesome and even grave symptoms, that we incline to agree with Freund,[8] who says: "I firmly believe that trichomonas is the direct cause of certain forms of acute, chronic and recurring enteritis, with abdominal pain, diarrhea, loss in weight, elevation of temperature and at times anemia." At the time (1908) when he made this statement he reported one case that died of progressive pernicious anemia and another less grave that recovered, although strongly suggesting the pernicious type of anemia.

While our group is too small to serve as a basis for statistical analysis, yet the suggested prevalence of these diseases in our community is worthy of attention. Also, the little group presents so many cases of striking individual interest, both as to course and treatment, that we have felt justified in discussing a few of them.

[6] Cited by James: Proc. Med. Assn., Canal Zone, vol. vi, part 1, p. 98.
[7] California State Jour Med., May, 1918, p. 240.
[8] Arch. Int. Med., 1908, No. 1, i, 28.

CASE I.—A mining engineer, aged thirty-six years, contracted amebic infection in Colombia and had been cured and had relapsed several times before coming under our notice. He was emaciated, anemic and running a temperature ranging from 99° to 102°. He was sensitive to pressure throughout the entire abdomen and had griping pain when the bowel moved. The stools were frequent and liquid, containing mucus, pus and blood, and showed under the microscope myriads of Ameba histolytica. This case presented the clinical picture of a severe amebic infection. The outlook was not promising and the progress at first was discouraging. However, with absolute rest in bed and careful attention to diet and nursing, he made a good recovery in about three months. He returned to the city about six months later, with a distinct relapse to all of his old symptoms, although they were not so severe. He was again treated much as before, with similar results, and after nine months has not again relapsed. This case we feel illustrates a not uncommon course of severe amebic infection treated in the most generally accepted manner, with emetin injections, ipecac by mouth and colonic saline irrigation. He relapsed because the encysted ameba were not all destroyed, and meanwhile he was a convalescent carrier of constant menace to those about him.

Case No.	Reported in detail.	Sex.	Age.	Place of original infection.	Clinical symptoms.	Protozoa.
1	r[a]	M.	26	South America	Dysentery	Ameba histolytica.
2	r	M.	23	Mexico	Dysentery	Ameba histolytica.
3	r	M.	43	South America	Hyperchlorhydria	Ameba histolytica; oxyuris; bothriocephalus; round-worm.
4	..	F.	35	United States	Dysentery	Ameba histolytica; trichomonas.
5	..	M.	65	.....	Achylia; diarrhea	Trichomonas.
6	r	M.	47	Philippines	Nervous exhaustion; hypochlorhydria	Ameba histolytica; trichomonas.
7	r	F.	43	Minnesota	Diarrhea; hyperchlorhydria	Trichomonas.
8	r	F.	47	Mexico	Fever; chills	Trichomonas.
9	..	F.	46	.....	.....	Trichomonas.
10	r	M.	68	Wisconsin	Anemia (pernicious?)	Ameba histolytica; trichocephalus.
11	r	M.	38	Mid-West	Intermittent diarrhea	Ameba histolytica; trichomonas.
12	..	M.	50	South Africa	Intestinal indigestion; constipation	Ameba histolytica.
13	..	M.	59	Mexico	Dysentery	Ameba histolytica; uncinaria; strongyloids.
14	..	M.	58	New Jersey	Dysentery	Ameba histolytica.
15	..	M.	40	North Carolina	Dysentery	Ameba histolytica.
16	..	F.	40	Nebraska	Constipation	Ameba histolytica and monads.
17	r	M.	37	Cuba	Attacks of somnolence	Ameba histolytica; trichomonas.
18	..	F.	65	Japan	Diarrhea; achylia	Ameba histolytica.
19	r	M.	43	Northern U. S.	Diarrhea	Trichomonas.

[a] r = reported at length in body of paper.

CASE II.—Male, Spaniard, aged twenty-three years, who had lived in Mexico, presented typical symptoms of acute amebic dysentery; acquired complete relief of symptoms under intravenous injections of emetin and kerosene enemata. Like Case I, the cysts persisted in the stools and were so recorded when he returned to Mexico against our advice.

CASE III.—A mining prospector, aged forty-three years, who had suffered severe malaria, with intestinal hemorrhages, while in Colombia, on his return to California sought relief for definite hyperchlorhydria symptoms. The blood examination, while showing no anemia, directed our attention to the bowel by a 7 per cent. eosinophilia. The stools on examination showed pin-worms, many ova of Bothriocephalus latus, an unknown species of round-worm and numerous Ameba histolytica. This man has had no dysentery since his malaria, and after his hyperchlorhydria was corrected by proper diet, he expressed himself as feeling well, and shortly afterward disappeared. He had been cleaned out with calomel and santonin and given a course of alcresta ipecac, with what permanent results we are unable to report. The case is quoted to illustrate the effect of intestinal intruders upon the blood and stomach glands as well as to show that a strong adult can carry about quite a lively fauna, with none of their characteristic symptoms in evidence.

CASE VI.—An army officer, aged forty-seven years, who had seen service in the Philippines, suffering both severe malaria and yellow fever, but not dysentery. Repeated stool examinations during the previous year had always shown trichomonas intestinalis hominis. He was nervous and generally run down, with a slight degree of anemia and a lowered gastric chemistry. The bowel was for the most part slightly constipated; abundant monads were found in the stools. He was persuaded to start his furlough with several weeks' rest and upbuilding treatment. Although ameba later showed in the stools, he markedly gained in every way, and is now at the end of a year actively engaged on the Western front. We were unable to learn how completely the protozoa were eliminated from the stools at the army hospital where he was later treated, but we feel that his transference to Northern latitudes would have a tendency to reduce their virulence. This case suggests the possibility of overlooking the ameba even when attention is directed to the stools by the presence of other parasites.

CASE VII.—An unmarried woman, aged forty-three years, teacher and housekeeper, from Minnesota, never had been in a tropical latitude. Complained of hyperchlorhydria symptoms and tendency to diarrhea for many years. The hyperchlorhydria was demonstrated by analysis, with some pylorospasm and a ptosed stomach. The stools contained monads but no ameba. Careful roentgen-ray study showed no evidence of ulcer. Her stomach symptoms gradually improved under proper diet and support of that

viscus. Under this treatment and intermittent courses of colonic flushings a normal physiological bowel function was established without any tendency to loose stools. We are inclined to look upon this case as one of chronic diarrhea, due to monad irritation.

CASE VIII.—A somewhat analogous case was an unmarried woman, aged forty-seven years. She had never been of robust physique, although in no sense an invalid. For the past ten years, dating from a visit to Southern New Mexico, she had presented occasional fever paroxysms, much like a malarial seizure, with marked chill followed by 1° to 4° of fever and marked sweating. This complete cycle would be repeated daily for three to five days and gradually disappear. A blood examination made during a chill showed a leukocytosis of 17,000, with a straight polynuclear advance to 95 per cent. No malarial plasmodia could be demonstrated at any of several blood examinations. Slight evidence of colitis, without any bowel looseness, directed attention to the stools, which proved on examination to be swarming with monads. In this case the monads could be made to disappear from the stools by the free use of calomel by mouth and mercuric chloride (1 to 20,000) flushings of the colon. After some months of observation we found that if the monads were allowed to return to the stools the patient would promptly suffer a return of her paroxysms, which were absent as long as the stools were monad-free. This patient is still under observation. Her stomach chemistry was that of a moderate hypochlorhydria, with a tendency to constipation. Methylene blue and thymol were tried without success in this case.

CASE X.—An American business man, still active at sixty-eight, a year ago applied for relief from obstinate diarrhea. He showed complete absence of HCl and ferments in the gastric juice, and his diarrhea for a time was relieved by suitable diet and the free use of dilute HCl. A few months later he became quite anemic and dyspneic and his bowel began to trouble him again. The blood showed a marked secondary anemia, obscurely close to pernicious in type, the red cells falling to 1,500,000, and with the color index constantly 1.5. The stool showed abundant Ameba histolytica and trichomonas. The kidneys and other organs except the stomach were negative. By keeping him at rest and controlling his diet this patient's blood was gradually built up to normal in about three months, cacodylate of iron being used liberally in deep gluteal injections. This may have helped in the fight against the ameba, although both emetin hydrochloride and ipecac in pill form were persistently used. In this case we are inclined to attribute the final disappearance of the ameba to the free use of salol-coated pills of powdered ipecac. A few monads have persisted in this case, more, we feel, because of the patient's refusal to be "fussed" with when once he felt well again. This man had never been in the tropics.

CASE XI.—An energetic American business man, aged thirty-eight years, complained of having had intermittent diarrhea most of his life, as had his father before him. He came from one of the Northern Middle West States and had never been out of the United States. His mild stomach symptoms were the expression of a moderate hypochlorhydria. The stools showed both Ameba histolytica and trichomonas in abundance. As he refused to rest he was treated throughout as an ambulatory case. He presented but little anemia and was in fair flesh and strength. Hypodermics of emetin followed by "Al Cresta" tablets cleared up the ameba, which were presumably not a very virulent strain. The monads also cleared up under the mercury treatment previously mentioned. Most of the monads we have met seemed to thrive in solution of methylene blue. At last reports about two months ago this case was apparently well. When compared with Case I it suggests the variability of virulence of these protozoa.

CASE XVII.—An American male, aged thirty-seven years, who had seen military service in Cuba and suffered from an epidemic of ileocolitis while encamped in Florida. He complained chiefly of having had for eighteen years lethargy, during attacks of which he would practically fall asleep while going about. The attacks would come on while working, riding horseback, talking, etc., and were fought off with great difficulty. Ameba histolytica and trichomonas were found in the stools. His somnolent attacks cleared up under emetin. Mild attacks recurred after three months and emetin was resorted to again and controlled the recurrence of his lethargic feeling. Two or three doses of the drug usually suffice for this purpose.

CASE XIX.—An American business man, aged forty-three years, who gave a history of recurring diarrheas extending over several years, attendant upon a general nervous breakdown. He had multiple diverticulitis, with general peritonitis and repeated abdominal abscesses. This case ran a long tedious course of abdominal trouble, with several operations to drain abscesses. As monads were early noticed in the stools we cannot resist speculating as to their possible role in the production of his trouble. Might not the monads have early produced an irritation which invited other infection?

In conclusion, we wish to lay stress on a few points:

1. San Diego County undoubtedly contains many cases of protozoal infection more or less active, as well as many convalescent carriers.

2. Some of these cases from Northern latitudes probably become more active by reason of the climatic change, the effect of a marked change of climate and latitude upon the virulence of protozoa having long been known.

3. All patients presenting obscure bowel symptoms, especially if anemic or achylous, should have the stools carefully searched for parasites.

4. The pathogenicity and behavior of the intestinal protozoa vary under different conditions of climate, latitude, exercise, diet and medicinal treatment.

5. The flagellates (monads) are capable of distinctly pathogenic behavior.

6. The most satisfactory treatment we have applied to the monads up to the present is the double mercury treatment above outlined.

CHRONIC JAUNDICE—FAMILY TYPE.[1]

By James I. Johnston, M.D.,

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Until a few years ago there was little published in regard to this type of chronic jaundice. In 1910 there was shown at the University of Toronto, to the members of the Interurban Clinical Society, a young man suffering from chronic jaundice, with enlarged spleen, which had existed since childhood, and with periods of exacerbation when the jaundice became more intense. There had been an uncle in the family who had suffered from the same condition, but neither one of them had been incapacitated in any way, and complained only of the persistent discoloration. This case shown was diagnosed as family jaundice, but no other analyses were brought to our attention. Since 1913 a number of articles have been written concerning this disease. The French writers are said to have reported on this affection more fully and elaborately than others, but now several American clinicians have reported cases. The best term to express the disease seems to be splenomegaly with or in chronic, congenital, hemolytic jaundice. The disease is exceedingly rare and its pathology is not understood. It is true jaundice and not pigmentation of the skin, such as occurs in Addison's disease or in what is known as Gaucher's disease, which is also a splenomegaly. As one of the terms of its name expresses, it is a hemolytic and not an obstructive jaundice. The disease clinically is characterized by the striking general chronic icterus, the large spleen, moderate anemia, good general health, and the possible history of more than one case in a family. The etiology of this disease is unknown, its pathology unexplained, and its entity recognition manifest by certain signs and symptoms together with blood and urine changes. There are two theories in regard to its manifest symptomatology as well as its cytologic analysis. One is that there is an imperfect formation of the blood, and the other is that the normal cells are unstable or fragile

[1] Read before the Pittsburgh Academy of Medicine.

and hemolysis follows, due possibly to the presence of unsaturated fatty acids in the blood or reduced cholesterin, which is inhibitive normally. The patient reported had a normal cholesterin content in the blood.

Some of the observers have suspected syphilis to be a causative hereditary factor, but the use of salvarsan has produced increased hemolysis and subsequent increase of jaundice. Others, on the basis that it might occur as an hereditary factor following tuberculosis, have used tuberculin with the effect of also increasing the hemolysis and inciting enlargement of the spleen. Some of the writers reporting cases have emphasized the presence of periodic abdominal pain associated with the patients' symptomatology, but in most cases it has proved to be pain due to gall-stones. My own case, which is reported below, presented no abdominal pain whatever, and no suspicion of gall-stones arose at any time. Thayer and Morris, in 1911, reported a case with this symptom present in whom no stones were found upon operation. Other writers report cases which, with abdominal pain, have had stones removed, the operation not giving absolute relief from this symptom; small stones in the liver ducts have then been suspected.

My own case is a man, aged twenty-three years, an American by birth, and employed as a moldmaker in the pottery works of an adjacent State. He was under my observation continuously for a period of ten days at the Mercy Hospital, having been referred to me by Dr. George L. Hays, and the man has reported to me since every few weeks. His sister, aged thirty years, also seen by the writer, presents exactly the same picture clinically, although no blood or urine examination has been made upon her. Their histories are practically the same, the man complaining only of a large leg ulcer besides the jaundice, ad the sister complaining of dysmenorrhea in addition to her icterus. They are otherwise well and live and work as the rest of us. The presence of uterine stenosis in the woman and a talipes equinus in the man may be suggestive hints of congenital factors present in both, some such factor producing the hemolytic jaundice. The chief complaint as stated was general icterus and the ulcer of the leg. He has been jaundiced as long as he could remember, certainly since ten years of age. It has been of equal intensity during this time except when the patient had what is said to have been an attack of malaria, when it became more intense. The diagnosis of malaria is doubtful. Ten years ago he was operated upon by the late Dr. R. W. Stewart, at the Mercy Hospital, for the talipes equinus mentioned before, and observations made at that time, with notes, show that the spleen was very large and the patient was jaundiced. This leg ulcer on the left side, the side formerly operated upon, first formed from a small pustule a few years ago, and later broke down, forming an ulcer which has gradually enlarged to a diameter of 2 cm. This ulcer was either due to a varix of the superficial

vein, superinduced by an old phlebitis following typhoid fever at fifteen years of age, or by pressure of the large spleen on the iliac vein.

Family history elicited states that his father is living and well at fifty-two years of age, and his mother died at fifty-two of an unknown cause. Two brothers and two sisters of adult years are alive and well; two children died in infancy; one sister, aged twenty-nine years, reported above, also suffered from this disease. This makes a family of six living children, two of whom are suffering from chronic jaundice. There is no history of carcinoma, cardiac or renal disease, tuberculosis or syphilis in the family. I had no opportunity to test the father for syphilis, such as was done with the patient. The man is a fairly well-nourished individual, showing no signs of serious illness. The skin is warm and soft, and is deeply jaundiced throughout. The pupils are dilated and react to light and accommodation sluggishly. The conjunctivæ are intensely jaundiced.

The oral hygiene was good and the mucous membranes were pale and jaundiced. The physical examination of the thorax was negative. The abdomen presented a unilateral distention on its left half, and the entire skin of the abdomen as well as the rest of the body was deeply jaundiced. The liver was slightly below the costa-border, while the spleen was greatly enlarged and explained the distention of the left hemisphere of the abdomen. This organ at this time, April 4, 1916, extended beyond the median line and downward to the brim of the pelvis, with the patient in an upright posture. The spleen also extended upward to the sixth interspace. The splenic notch could be felt 5 cm. below the umbilicus. The urine shows no clinical abnormalities save the presence of urobilin and the absence of bile; it is therefore an acholuric jaundice. The stools are normal in color, indicating the normal presence of bile and not pointing to obstruction to the biliary ducts. The blood shows a moderate grade of secondary anemia, the hemoglobin was 45 per cent., the red-blood cells 3,150,000, and the white-blood cells 11,000. The differential count was proportional. The polymorphonuclear count equalled 77 per cent. The reported cases do not show a leukocytosis, but the leukocytic count is explained by the presence of the leg ulcer. The blood Wassermann was negative. The chronic jaundice occurring in two members of the family, the large spleen, the absence of bile in the urine with urobilin present, and the secondary anemia were the basis of our diagnosis.

The consensus of opinion among clinicians at present seems to be that these cases are very suitable for splenectomy, as the internal secretion of a pathological spleen when plus favors hemolysis, but it would be inexpedient and hazardous to remove a spleen of this size. Heretofore these cases have been treated by iron and arsenic and by the roentgen rays. This patient was treated by roentgen rays once a week, with the hope of reducing the size of the spleen preparatory to a splenectomy. When last seen the spleen, after weeks of roentgen-ray treat-

ment, had been reduced to about two-thirds of its former size, with an increase in the jaundice and in hardness of the consistency. Whether we shall succeed in arriving at a suitable stage is doubtful, but should the spleen be reduced to a manageable size this operation will be urged upon the patient. A prominent clinician recently stated at a public gathering that while he himself would not submit to splenectomy for pernicious anemia, he would have this operation done for chronic congenital family icterus. The after-effects have been striking in some cases, the jaundice entirely disappearing. In the acquired family jaundice the fragility of the cells has been corrected and their normal resistance to hemolysis has been restored; but in the congenital family icterus the cells never regain their normal resistance. The reticulated red cells, of which there is normally 1 per cent. in the blood, looked upon by some observers as indicative of destruction, are probably an indication of regeneration, rising from 5 to 20 per cent. in this disease. The coagulation time and the grade of hemolysis unfortunately were not tried out in this case. Aside from the histological study of the removed spleen the diagnosis could hardly be questioned.

THE PRINCIPLE OF BLOOD GROUPING APPLIED TO SKIN GRAFTING.

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Grafts may be classified as *autografts*, where the skin is transplanted from the same individual; *isografts*, where the skin is obtained from another person; and *zoögrafts*, where the graft is taken from one of the lower animals. All observers agree that the autograft is the most satisfactory, that a permanent take is least likely or impossible to obtain with zoögrafts, while such uncertain results are obtained with isografts that many surgeons have been led to abandon their use.

With the use of isografts, whether partial or total thicknesses of the skin, a peculiar phenomena has frequently been observed. In the course of the second to the fourth week a certain percentage of these apparently healthy primary takes begin a slight desquamation of the epidermis, then they show signs of resorption by becoming smaller, paler and thinner, and shortly are either reduced to a mere bluish pellicle or have completely disappeared. The grafts apparently fade or melt away little by little. Having had similar experiences, and having seen the uniformly successful results obtained in blood transfusion with matched blood, it occurred to me that the

permanent success of isodermic grafts might be dependent on the same underlying principles.

The present status of blood grouping may be briefly stated as follows: Based on the interaction of serum or plasma and red blood cells, each individual is placed in one of four groups. This classification, as stated by Moss, is as follows:[1]

Group I. Serum agglutinates corpuscles of no person.
Corpuscles are agglutinated by serum of Groups II, III and IV.

Group II. Serum agglutinates corpuscles of Groups I and III.
Corpuscles are agglutinated by serum of Groups III and IV.

Group III. Serum agglutinates corpuscles of Groups I and II.
Corpuscles are agglutinated by serum of Groups II and IV.

Group IV. Serum agglutinates corpuscles of Groups I, II and III.
Corpuscles are agglutinated by serum of no person.

Groups I and III are rare groups; Groups II and IV are common. The relative incidence of the four groups, as found by Karsner[2] in 1000 groupings, was: Group I, 3.1 per cent.; Group II, 42.4 per cent.; Group III, 8.3 per cent.; Group IV, 46.2 per cent.

In the transfusion of blood one remembers that the important point is the effect of the patient's plasma on the cells to be introduced. What then can be expected in the transplantation of skin? If one substitutes the term "skin graft" for the "cells" in the above table, like effects may be looked for. It can be readily seen then that if a skin donor is used in the same blood groups as the recipient to be grafted, or if autodermic grafts are used, no resorption of the graft should occur. Going still further with the simile, and adopting the suggestion advanced by Lee[3] and upheld by general usage, that as Group IV blood donors may be used for patients belonging to any of the four groups, because in actual transfusion agglutination does not occur in either direction, so in skin grafting permanent takes may be expected from this "universal door" class. Such was our experience in every instance. That is, while initial takes were recorded with skin from donors of all four groups, on recipients of all four groups, only autodermic grafts and matched isografts, including Group IV donors, remained permanent takes and continued to grow and expand.

One donor from each of the four blood groups was used for every grafting. Usually all four groups were represented among recipients, and were used as donors of grafts as well. In each

[1] Moss, W. L.: Simplified Method for Determining the Iso-agglutin Group in the Selection of Donors for Blood-transfusion, Jour. Am. Med. Assn., 1917, lxviii, 1905.

[2] Transfusion with Tested Bloods, Jour. Am. Med. Assn., 1918, lxx, 760.

[3] A Simple and Rapid Method for the Selection of Donors, British Med. Jour., 1917, ii, 684.

instance the bloods of both donors and recipients used in the skin-grafting experiments were tested according to the simple and rapid method recommended by Lee, using serums of individuals of Group II and III originally furnished this Base Hospital by Major Lee. In every case Group IV serum was used to check up the results.

For the sake of comparison, Thiersch grafts were used in the first half of the cases and Wolfe grafts in the latter half, with no difference noted either in the primary or the permanent "takes." The long strips of skin thus secured were cut into sections, as recommended by Douglas, Colebrook and Fleming,[4] and either grafted on at once or wrapped in gauze moistened with warm saline until ready for use. An hour was the greatest delay in the latter instance.

As the problem at hand concerned itself entirely with the fate of skin grafts from donors of the four groups, no effort was made to completely cover the exposed areas. Specimen grafts from the same donor or donors of the same blood groups were placed in close proximity to each other, and always one or more of them were near to the margin of the patient's own ingrowing new skin. Careful tracings and notes were kept of the position and progress. We regarded as *primary takes* only those that attached themselves to the surface by epithelization. *Primary failures* were those that did not attach themselves and no epithelial growth remained behind.

In the further progress the primary takes pursued one of two well-defined courses: the first, representing biological compatibility, continued to grow and obviously became a permanent part of the anatomy; the second, representing a biological incompatibility, after a brief period of promise became pale, edematous and gradually faded out, sometimes being cast off as a scale. This might occur any time up to a month or more.

The foregoing is based on observations of 26 different patients, 17 of which are available as evidence. These were successfully grafted with sections of skin from each of the four groups and with autografts. Of these 17 cases, 2 were members of Group I, 8 were in Group II, 2 in Group III, and 5 in Group IV.

Group I. Case 1. Amputation stump. Preceding grafting, the stump was ionized daily with 1 per cent. sodium chloride and 1 per cent. zinc sulphate by Captain Baker-Young, R. A. M. C. The grafts of all the groups and the autograft showed initial takes and all continued to increase in size and to be healthy in appearance when the patient was evacuated twenty-three days later. (See Group I, Case 1.)

Case 2. Tangential shell wound in the region of the left knee. On the twenty-third day after being wounded the granulating sur-

[4] On Skin-grafting: A Plea for its More Extensive Application, Lancet, London, 1917, excii, 5.

face was covered with a section graft from each group and one autograft. Seven days later all of the original grafts except that of Group III, which was accidentally removed with the first dressing, were still on. Primary takes of all the remaining groups were present on the eighteenth day. On the twenty-eighth day all grafts had continued to grow as permanent takes and were connecting up with one another and with the patient's own marginal skin growth.

GROUP II. Case 1. Amputation stump. Thiersch skin grafts from donors of each of the four groups and from the recipient himself were applied to the stump surface on January 27, 1918, and again two weeks later. Following neither operation did a Group I, III or autograft take, while strong firm skin was obtained with another Group II and a Group IV in the first and with a different Group IV in the second instance, all of which had continued to grow and increase in size up to the time of evacuation, twelve days later.

Case 2. Amputation stump. Autografts and grafts from donors of each of the four groups were grafted on the stump surface and all took. Between the eighteenth and twenty-third day the Group I and III graft takes grew rapidly smaller and fainter and finally disappeared. Takes from two different Group IV donors and one from the recipient were firmly established and growing when the patient was evacuated twenty-five days later.

Case 3. Amputation stump. One isograft from each of the four groups and one autograft were put on and all had established takes thirteen days later. During the four weeks preceding evacuation the Group I and III grafts diminished to almost pin-head size while the Group II and IV and autograft had more than doubled in size and were firm and healthy. (See Group II, Case 3.)

Case 4. Amputation stump. Surface grafted with several sections of skin from each of the groups and from himself. Takes from all groups were present two weeks later. By the eighteenth day, however, the Group III were faded out. The Group I take gradually decreased in size during the first three weeks, then remained stationary in size for two weeks more, while the recipient's own proliferating epithelium surrounded it and during the sixth week was cast off as a dry scale, leaving takes from two different Group II donors; two different Group IV donors and an autograft growing.

Case 5. Amputation stump. Autografts and grafts from all the groups made primary takes. Group III takes from two different donors became steadily smaller and faded out after three weeks. During the fourth week the Group I take, which had decreased in size, became film-like and disappeared. When evacuated on the thirtieth day only members of Groups II and IV were on. These had steadily increased in size and in one large area had joined up with one another and with the recipient's own surrounding ingrowing skin.

Case 6. Amputation stump of left thigh was grafted with his own and with skins from donors of the four groups. Only autografts took.

Case 7. Amputation stump. Autografts and section of skin from all four groups put on stump a week later. Only autografts became established.

Case 8. Gutter wound of right thigh was grafted with two Group III and one Group II graft five weeks later. Only the Group II graft was a permanent take.

GROUP III. Case 1. Grafts from all groups and autografts were applied on an amputation stump surface. All took. Grafts of Group I and II decreased in size and disappeared during the fourth week. When discharged at the end of the seventh week two Group IV, one Group III and one autograft remained as permanent takes. (See Group III, Case 1.)

Case 2. Amputation stump surface grafted with skin from a donor of each of the four groups and with autografts, but only one autograft was a permanent take. The grafting was repeated a month later, using all groups, but only Groups III, IV and autografts took. When evacuated one month after the second operation two Group III grafts, one Group IV and two autografts remained as permanent takes.

GROUP IV. Case 1. Shell wound of left thigh. Had two severe secondary hemorrhages and was given 750 c.c. of blood of his own group (Group IV) each time; amputation was done after the second. Forty-six days after injury a thick autograft was removed and applied on the stump, along with similar pieces of skin from donors of each of the four blood groups. In ten days takes from all groups were healthy, large and nearly as thick as the original grafts. From the seventeenth day on to the thirtieth, Groups I, II and III began to shrink and grow steadily thinner and paler. When evacuated on the forty-second day, Groups I, II and III had nearly disappeared while the autografts and isogroup grafts were large, thick and healthy, and in the case of the former were being incorporated with the patient's own ingrowing skin.

Case 2. Extensive burns of the inner aspect of the right thigh from shell explosion. Section grafts from the recipient and from donors of each of the four groups were applied. All of these grafts took and continued to grow equally well for three weeks, when in the course of a few days the members of Groups I, II and III became thin and pale and faded away, leaving only several strong Group IV and autografts behind, which continued to be healthy and increase in size until the twenty-eighth day, when the patient was evacuated. (See Group IV, Case 2.)

Case 3. Amputation stump. Grafts from the four groups and from the patient himself. The original grafts of skin were off and found to be replaced by strong healthy takes two weeks later. About

the twentieth day the Group III primary takes began to resolve and were off a few days later. During the fourth to the seventh week the Group I and II grafts appeared to shrink in size, but at the same time they joined up each with the adjacent skin of the same group. By the seventh week the grafts of Group I had grown very small, while two of Group II came off, leaving the third as a minute pale island. In the meantime three of the Group IV grafts and the autograft extending rapidly by peripheral growth joined one another and at the time of evacuation, the beginning of the ninth week, had covered nearly a quarter of the stump surface.

Case 4. Amputation stump. Autografts and grafts from several different donors of each of the four groups were put on the stump surface. Of these one each of Group I, II, III, two isogroup IV and two autografts took. The Group I and II takes disappeared rapidly during the following week, leaving large flourishing Group III and IV grafts. During the last of the seventh week the Group III graft suddenly became pale and disappeared in the course of a few days. When evacuated eight weeks after being grafted only autografts and isografts remained, and these had joined up by peripheral extension and were normal in appearance.

Case 5. Large tangential shell wound of right deltoid. Grafted two weeks after injury. Section autografts and grafts from each of the four groups were used. All were established ten days later. The Group I and II takes had disappeared by the twentieth day and the Group III take during the last of the fourth week, leaving one Group IV graft and two autografts.

Initial takes occurred independently of group compatibility; but *permanent takes* were modified by biological compatibility as follows: Group I patients grew skin from donors of each of the four groups and equally well. Group II grew isogroup grafts and grafts from Group IV, while primary skin takes from Group I and III donors in the course of time either shrunk to minute size or entirely disappeared. Group III recorded only skin from the same group and Group IV as permanent takes. Permanent takes from the same group only were obtained in the case of Group IV recipients.

SUMMARY. 1. Autografts grow best.

2. Isografts obtained from donors of the same blood group as the recipient or from Group IV donors became permanent takes and grew almost if not equally as well as autografts.

3. Isografts where the donor and recipient were of different groups did not remain as permanent growths except when Group IV skin was used or when the recipient was a member of Group I.

4. Group I recipients grew permanent skin from donors of all of the four groups and apparently equally well.

5. Group IV skin grew permanently on recipients of all groups, but only Group IV grafts and autografts remained as permanent takes on Group IV recipients.

6. It appears that skin grafting obeys the principle of blood grouping, as in the transfusion of blood.[5]

I desire to render thanks to Colonel Meek, R. A. M. C., Colonel Pilcher, R. A. M. C., Colonel Crile and Colonel Lower, M. C., U. S., for facilities given for this investigation; to Captain Karsner, Captain Eisenbrey and Lieutenant Richardson, M. C., U. S. A., for doing the laboratory work; and to Sergeant Brownlow, who made the illustrations; also to the entire staff of this Base Hospital, whose coöperation is greatly appreciated.

THE DIFFERENTIAL DIAGNOSIS BETWEEN MITRAL STENOSIS AND AORTIC INSUFFICIENCY.

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The fact that certain cases of mitral stenosis exhibit a diastolic murmur at the base and certain cases of aortic insufficiency exhibit a presystolic murmur at the apex makes the differential diagnosis between the two conditions a matter of some difficulty and of great interest. In pursuing the study of the cases of mitral stenosis and aortic insufficiency seen in the draft examinations, we outlined a routine which we endeavored to follow in each case. This routine included history, location and character of the apex-beat, including thrills, the outline of the cardiac borders with reference to the mid-sternal line, the location and characteristics of the murmurs, blood-pressure studies with arm by the side, arm above the head (patient standing), pressure (recumbent) in the leg and in the arm, vascular signs, including Corrigan pulse, capillary pulse, Traube's sign and Durossiez's sign.

Two questions we have put to ourselves to answer: (1) What is the criterion or what are the criteria which help one in the differential diagnosis? (2) How frequently does it become necessary to distinguish between mitral stenosis with a Graham-Steell murmur and an aortic insufficiency with a Flint murmur?

History, upon which so much importance is laid in civil life, helps us very little with the draft cases. We have found two types of histories: (1) that of severe rheumatic fever in individuals with perfectly normal hearts who do not wish military service and who know how much emphasis is laid on a history of this nature, and (2) that of perfect health throughout their lives given by individuals with

[5] While completing this report, two suggestions as to the desirability of using matched skin grafts have come to my notice: Davis, J. S.: Some Problems of Plastic Surgery, Annals of Surgery, July, 1917, p. 89. Masson, J. C.: Skin Grafting, Jour. Am. Med. Assn., 1918, lxx, 1581.

badly damaged hearts who want to serve. The latter type complain of no symptoms and insist that they have sound hearts, but who finally admit, when told that they are absolutely disqualified, that they have had heart trouble for a long time. Therefore, we are inclined to discount the anamnesis. Stress is often laid on the fact that if there is a rheumatic history the mitral valve is affected, if a syphilitic history, the aortic. How untrue this is those who have had large experience in cardiovascular work will testify. At all events, in our 11 cases of aortic insufficiency which we have carefully studied, rheumatism occurred 4 times in the history, syphilis but once and in 6 cases there was a history of neither. However, in these army cases it is unwise to lay too much emphasis on what the individual states, and reliance should be placed on what the examiner himself finds.

Visual and Palpatory Findings. 1. *Apex-beat.* The apex-beat is displaced to the left beyond the 9 to 10 cm. generally held to be normal, and may be in the fifth or sixth intercostal space. (The circumference of the chest and the weight of the individual have some influence on the location, however). There is a tumultuous movement to the impulse, which is not the quick circumscribed beat of a mitral stenosis but extends widely and imparts itself to the left chest wall, which reflects the forceful systole. On palpation the apex-beat humps itself under the hand and the contraction is felt for some time, while in a stenosis the apex-beat is suddenly felt as a single tap, which recedes quickly and does not linger under the palm. Even if there is a thrill in both instances the apex-beat of a stenosis, as we have found it in the draft, is a forceful circumscribed tap or shock, which quickly strikes the hand, being clearly felt, but which as quickly falls away. On the other hand, the apex-beat of an insufficiency is a heave of great force, of extended area and of considerable duration in its contact with the palm, writhing back to rest for the next upheaval. No distinction can be made between the thrill of a stenosis and that of a Flint, and if there is mitral insufficiency as well as stenosis, the location and character of the apex-beat are of little assistance in the differentiation of the two conditions.

2. *Cardiac Outline.* In all cases of aortic insufficiency that we have examined there has been marked hypertrophy of the left ventricle, while in the pure stenosis (no insufficiency) there has been no hypertrophy, or but slight if any. When mitral insufficiency is present, hypertrophy is generally seen, though not to the extent found in aortic insufficiency. The average width of the left ventricle in the aortic cases has been between 11 and 12 cm. from the midsternal line. Cabot lays emphasis on the cardiac hypertrophy at autopsy, which is a finding to be expected, but he does not distinguish, in this respect, between a stenosis simplex and a stenosis with an insufficiency. He claims that one cannot rule out mitral stenosis with insufficiency because there is good evidence of left ventricular

hypertrophy, which is true so far as his autopsies show. It is not wholly true and scarcely partly true of pure mitral stenosis as it occurs in young males, who, as a matter of fact, show but slight if any hypertrophy. Therefore, I am impressed with the absence of hypertrophy as a valuable sign in differentiating between mitral stenosis and aortic insufficiency.

3. *Vascular Signs.* Special attention has been paid to the question of markedly pulsating vessels, Corrigan pulse, capillary pulse, Traube's sign, Durossiez's sign, blood-pressure in the arm and in the leg, persistence of the fourth phase in auscultatory blood-pressure determinations.

(*a*) *Pulsating Vessels.* In the cases of aortic insufficiency which we have examined, marked pulsation of the carotid, radial, brachial and axillary arteries has been a striking feature. Head-nodding has been noted in a few cases, but this seems to be less pronounced in the draft cases than in the advanced cases of a civil clinic. In mitral stenosis this marked vascular pulsation is inconspicuous or absent.

(*b*) *Corrigan Pulse.* A pulse of a Corrigan type is by no means an uncommon feature of diseases other than aortic insufficiency. It has been found in mitral stenosis, but never to the degree that it has been observed in aortic insufficiency. It was present in all our cases (11).

(*c*) *Capillary Pulse.* This is a difficult sign to elicit. The methods in vogue are: (1) To observe the pulsation under the finger nails following pressure. (2) To rub the forehead and look on the irritated area for alternate blushing and pallor. (3) To evert the lower lip and observe the pulsation through a glass slide pressed on the mucous membrane. The first two methods often fail, the third is the best, but glass slides are not always obtainable, so for this reason I have adopted the following procedure, which is simple and yields good results: With the subject facing the light, the lower lip is grasped between the thumbs and forefingers of each hand, gently pulled down and stretched so that the junction between the mucous membrane and the skin becomes whitened. Holding the lip in this position one can readily see a capillary pulsation if present. It was observed nine times in our 11 cases.

(*d*) Traube's sign was present eight times. To obtain a systolic tone in the arteries we have found it useful to listen over the brachial artery at the bend of the elbow with the arm extended above the head. In the cases in which the Traube sign was not elicited in the iliacs a tone could sometimes be detected in the brachial by this method. It is really an audible Corrigan pulse if one may so express it.

(*e*) Durossiez's sign was present but twice and is of little help in the diagnosis.

(*f*) Blood-pressure in the arm and the leg. The marked difference

between the systolic pressure in the arm and in the leg in aortic insufficiency has been offered as a diagnostic point of great value. Our findings are as follows:

Arm.	Pulse-pressure.	Leg.	Pulse-pressure.
150–42	108	210–0	210
170–30	140	258–0	258
134–62	72	182–70	112
200–70	130	270–115	155
138–36	102	270–0	270
188–28	160	270–0	270
178–86	92	290–0	290
140–90	50	162–115	147
135–65	70	168–82	86
136–56	80	172–56	116

Comparing these with 10 cases of mitral stenosis taken at random from our series we find:

Arm.	Pulse-pressure.	Leg.	Pulse-pressure.
116–68	58	138–80	50
122–84	38	160–100	60
135–80	55	168–84	84
120–80	40	168–90	78
122–62	60	148–75	73
155–85	70	178–110	68
138–70	68	150–88	78
136–80	58	158–92	66
152–95	57	176–98	68
115–75	40	156–88	68

There is in the mitral stenosis cases a difference between systolic pressure in the arm and the leg of 40 to 50 mm. Hg. In the aortic cases the difference may be as much as 130 mm. Hg. and in certain cases leg pressure is double that in the arm. When there is a difference over 60 mm. Hg. the lead is toward aortic insufficiency, although if below 60 there is no certain proof that aortic insufficiency does not exist.

(*g*) Pulse-pressure. Of equal importance, if not of more value, I believe to be the high pulse-pressure. The average pulse-pressure in health is between 45 and 55 mm. Hg. By examining the above table the high pulse-pressure in the arm and leg in aortic insufficiency is in marked contrast to the pulse-pressure in cases of mitral stenosis.

4. *Auscultatory Signs.* The murmur of an aortic insufficiency may be heard to the left of the sternum as well as in its normal habitat to the right of the sternum, so one is not particularly assisted from the standpoint of location. The Graham-Steell murmur is always heard to the left of the sternum. The character of the murmur is of little assistance, as that of aortic insufficiency may closely resemble that of the Graham-Steell. The latter murmur, however, is a localized murmur and is seldom transmitted beyond its area of production, whereas an aortic murmur is generally transmitted down the sternum.

The apical murmurs of an aortic insufficiency and a mitral stenosis may resemble one another, but there is this difference, that the Flint murmur is associated with a thumping, thudding first sound, whereas the true presystolic murmur of a mitral stenosis is followed by the snappy first sound.

The Flint murmur was present in our series twice in 11 cases (18.1 per cent.), and the Graham-Steell has been found twelve times in 36 cases (33.3 per cent.). A differential diagnosis of considerable interest if not of great importance from the practical side (as in either event the recruit should be rejected) must be made in quite a large number of cases.

CONCLUSIONS. The differential diagnosis rests on the findings revealed by inspection, palpation and percussion, with the auscultatory findings, excepting the quality of the first sound at the apex, holding a subordinate place. The most important features in favor of the diagnosis of aortic insufficiency (not arranged in the order of importance) are: (1) Displacement of the apex-beat. (2) Heaving feel of the apex impulse to the palpating hand. (3) Hypertrophy of the left ventricle. (4) Vascular signs, *i. e.*, marked pulsation of vessels, Corrigan pulse, capillary pulse, systolic tone in brachial, with arm above the head. (5) Blood-pressure increase of pulse-pressure, marked discrepancy between the arm and the leg pressures.

In favor of a mitral stenosis are—

1. Loud snappy first sound at the apex unless marked by an insufficiency of the mitral valves.
2. Absence of apical displacement and of cardiac hypertrophy.
3. Systolic tap or shock to the palpating hand.
4. Absence of vascular signs.
5. Absence of any characteristic blood-pressure phenomena.

THE CARDIOTHORACIC RATIO: AN INDEX OF CARDIAC ENLARGEMENT.

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THE question of heart size, especially in its relationship to hypertrophy and dilatation, is important to the civilian as well as to the military physician. Its knowledge is necessary in the diagnosis and interpretation of certain systolic murmurs as well as in the prognosis of cardiac, nephritic and vasosclerotic conditions.

For example, a systolic murmur at the apex, with the definite knowledge of cardiac enlargement, will certainly differentiate an

actual valvular insufficiency (endocarditic or myocarditic) from a functional murmur. Without such knowledge an accurate diagnosis is often impossible.

Let us see how important this knowledge of the size of the heart would be in prognosis. To illustrate this we need not go very far. For instance, a case of chronic nephritis with cardiac enlargement is surely of graver significance than without it. The same might be said of cases of hyperthyroidism in which cardiac enlargement would indicate permanent damage to the heart by the thyrogenic poison. Thus one might go on indefinitely with such examples. Suffice it to say, however, that enough instances might be found to warrant investigation into problems that might yield us a method of exact, yet simple determination of the cardiac size.

Cardiac hypertrophy and dilatation are terms frequently used though seldom verified except in conditions of extreme enlargement. Errors in this direction are common enough to justify us in the opinion that many a diagnosis is confused because the method of estimating the heart's size is faulty. This fact was brought out quite strikingly when the writer was engaged in heart work in the Army.

The physician in private practice relies upon percussion for the determination of cardiac size. But to percuss out a heart accurately for diagnostic purposes requires fine technic and is, at best, difficult, especially when slight or moderate enlargement exists. In fact, the London School of Cardiologists denies its possibility altogether even by the most expert. Personally, I cannot accept this extreme viewpoint. To me it seems that much information may be obtained by careful percussion of the heart. I must admit, however, the difficulty occasionally experienced and the great possibility of error.

The location of the position of the apex-beat for the same purpose has recently been reclaimed by Thomas Lewis and his disciples. Our experience on this point has shown us that the reliability of this sign as an index of cardiac enlargement is only moderate. It is of no help in early cases in which the apex-beat is little if at all displaced. This much may be said: (1) that cases of marked enlargement will cause displacement of the apical impulse to the left of the midclavicular line and sometimes downward; (2) that in spite of cardiac enlargement, such as must exist in definite forms of aortic regurgitation, the apex-beat is often within the midclavicular line; (3) that widely diffused apex-beats, as often occur in thin, nervous individuals, frequently seem outside of the midclavicular line even though the heart be unusually small; (4) that occasionally the point of maximum intensity cannot be located because of the diffusion of the apex-beat.

The other methods of investigating the heart's size are the instrumental ones. They consist of polygraphy, electrocardiography and orthodiography.

The polygram is occasionally useful in the determination of right ventricular hypertrophy. In this condition the outstanding feature is the retraction or negative type of apical pulsation. (See Fig. 1.)

But this can usually be visualized on the chest, so can the retraction of the third, fourth and fifth interspaces on the left side and the negative type of epigastric pulsation. By physical examination as much information is elicited as by the polygraphic studies. Thus the usefulness of the latter is minimized.

The electrocardiogram is very reliable. Enlargement of the auricle is evidenced by an increase in the size of the *P* wave. Hypertrophy of the ventricles is indicated by the downward displacement of the *R* wave in one lead and the lessening of its amplitude in another direction. Thus in right ventricular hypertrophy, such as in a case of mitral stenosis, one would get such a tracing. (See Figs. 2, 3, 4, 5, 6, 7.)

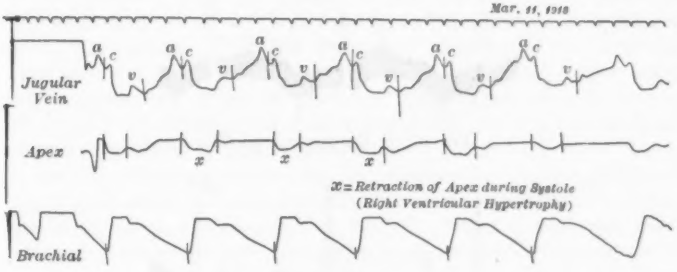

FIG. 1

The disadvantage, however, is that electrocardiography, which requires special training and technic, is not within the reach of the average practising physician. It must be repeated here that we started out to find a simple and easily applied method that should be sufficiently accurate for scientific diagnosis.

Hence we come to the orthodiagram or the roentgen-ray plate taken with the tube at six feet or more from the patient. This distance is chosen because of the divergent or enlarging effect of roentgen rays which occurs when the tube is placed nearer the patient than six feet. At this distance the rays become parallel, thus casting a true image of the heart on the roentgen-ray plate.

This method is simpler and quicker than the original orthodiagraph of Levy-Dorn and Groedel.

The roentgen-ray image of the heart is then perpendicularly bisected and the distance to the right and to the left of the median line is recorded. Thus we say the left border is 8 cm. and the right 3.5 cm. from the midline.

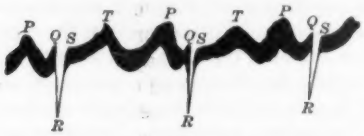

FIG. 2.—*R*, downward in Lead I.

FIG. 3.—*R*, small in Lead II.

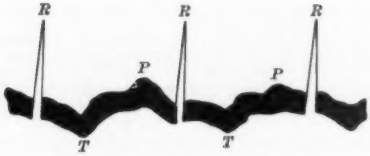

FIG. 4.—*R*, Upright in Lead III.

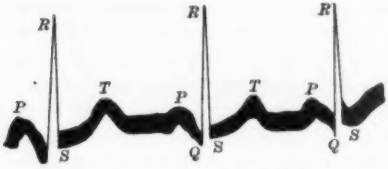

FIG. 5.—Left ventricular hypertrophy. *R*, upright and large in Lead I.

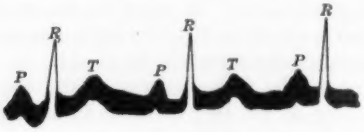

FIG. 6.—*R*, smaller in Lead II.

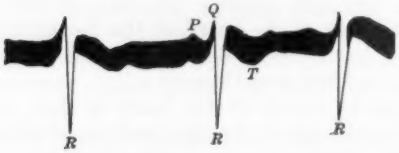

FIG. 7.—*R*, inverted in Lead III.

This method, though apparently reliable, is objectionable because there are no absolute standards for normal individuals with which to compare the resultant figures. Some text-books, however, give 4.4 cm. to the right and 9.1 cm. to the left as the upper marginal limits. I cannot agree with them, because I have seen absolutely normal hearts in which the left borders were as much as 13 cm. from the midline, while in cases of chronic valvular disease with undoubted hypertrophy corresponding diameters from 7.5 to 9 cm. were not rarities. Although paradoxical on the surface, its truth was many times emphasized on the writer.

This leads us to the question of the comparison of the cardiac diameters before and after the onset of valvular disease. If this were practicable, it would certainly tell us whether or not the heart in question was enlarged. For example, an adult develops rheumatic fever and the roentgenogram shows the left cardiac border to be 8.5 cm. and the right border 4 cm. from the midline. He develops in the course of his illness mitral valvular disease. Two years later the orthodiagram shows the l. b. to be 9.5 cm., and the r. b. 4.5 cm. from the midline. Thus the transverse diameter of the heart has increased 1.5 cm. It is apparent that a hypertrophy has taken place, principally of the left ventricle. Such information in the case of a systolic murmur heard at the apex would help a great deal in the diagnosis and the prognosis of the same.

Perhaps this question is being overemphasized in this article. If so, it is because of the numerous errors seen especially in military practice, where the diagnosis of mitral valvular disease was made altogether too frequently; certainly more so than is warranted by the lessons learned at the autopsy table. Also the diagnostic differentiation between the organic and the functional systolic murmur by the usual methods is inadequate.

In discussing comparative measurements of the cardiac diameters on the roentgen-ray plate before and after the onset of the heart affection I have chosen an adult for an example.

In a child whose heart is naturally growing, comparative measurements would be less valuable, because here an increase in the diameters could not be interpreted as indicative of hypertrophy.

Inasmuch as comparative mensuration such as was described would not be practicable, have we any other means of comparative measurement that could be of help? This calls for an affirmative reply.

It is based on the fact that the heart bears an almost constant relationship to its surrounding framework, the chest. This is seen in the narrow vertical type of heart found in association with the long status asthenicus chest. (See Fig. 8.)

The wide emphysematic chest has a heart of corresponding breadth and one which is more transverse and at a higher level than in the status asthenicus type.

These are the two extremes. Between them are numerous intermediary gradations. The outstanding feature in all of these is the parallelism between the form of the heart and that of the chest, as well as the constancy of the ratio between the transverse cardiac diameter and that of the thorax. (See Fig. 9.)

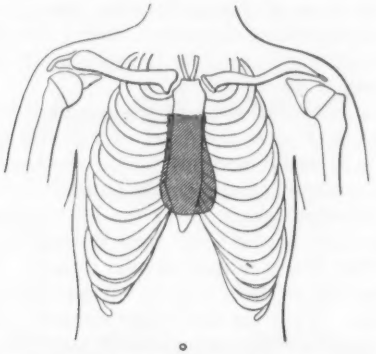

FIG. 8.—Heart, vertical, narrow "drop heart, found in status asthenicus.

It follows, then, that the newborn child, destined to be a person of asthenic proportions, will have a long tube-shaped or "drop" heart, which is the more primitive heart embryologically. The latter

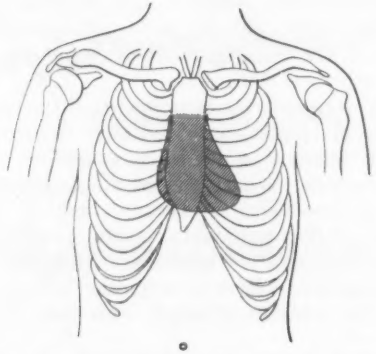

FIG. 9.—Heart, broad type, characteristic of habitus emphysematicus.

is more closely allied to the single tube from which the embryonic heart develops. Likewise the child with an emphysematic predisposition will have a heart that is in proportion to its wide chest.

This relationship is very constant, because of the parallelism in the growth of the heart and that of the chest wall. The only time

there is any divergence at all is during childhood. Then the heart is a little wider proportionately, more round and lies more transversely than in the adult.

This, however, does not limit the scope of application of the relationship of the heart to the thorax for diagnostic purposes. The heart diameters in children have been studied by Sawyer[1] and Voith.[2] With their results as a basis, deviations from normal can be detected in children by comparison with the figures of the above authors.

The former found in his study of 500 young children that the apex was outside of the mammillary line in 63 per cent. of the cases. Voith, as the result of his studies, says that the hearts in children are apt to be rather right sided, the distance to the right of the median line being 50 per cent. of that to the left. In adults, of course, the right diameter is less than 50 per cent. of the left.

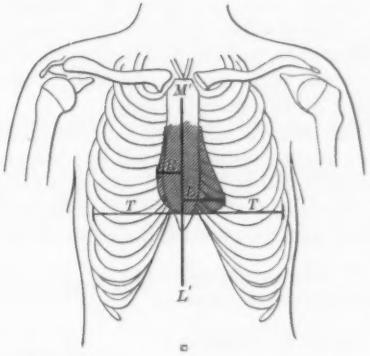

FIG. 10.—*M L'*, midline; *R*, from *M'L'* to right border (fourth space); *L*, from *M'L'* to left border (fifth space); *R* + *L*, *T. H.* (transverse diameter of heart); *T.T.* (transverse diameter of thorax); *C.T.* (cardiothoracic ratio) = $\frac{T.H.}{T.T.}$

Hence, in children we expect a high figure for the cardiothoracic ratio and the right side is slightly more prominent than in adults.

Then for practical purposes we may say that ratio between the size of the heart and chest is quite constant except when pathological processes set in. Then the relationship is disturbed, *e. g.*, the onset of valvular diseases will cause an enlargement of the heart without any accompanying change in the size of the chest. Thus it is seen that cardiac enlargement will show itself as an increase in the cardiothoracic ratio, if the latter is obtained by dividing the transverse diameter (right and left diameters) of the heart by that of the thorax taken at a given level.

Therefore, we studied a sufficiently large number of cases in order

to establish the normal ratio. We also had to determine at what level we would take the chest measurement.

We finally decided on taking the thoracic measurement at its greatest diameter, which is usually at the level of the apex or one space lower and measuring to the inner borders of the ribs.

The cardiac measurements were also taken at their widest points. Usually it was the fifth space on the left side, the fourth space on the right. We used the metric scale. (See Fig. 10.)

A word ought to be said concerning the taking of the plate. The patient should be in the upright position and breathing should be shallow. The operator should wait until the initial excitement of the patient passes off. If this precaution is not heeded the cardiac excursions between systole and diastole will be great enough to cause an appreciable difference in the measurement of the heart therefore in the cardiothoracic ratio and in the interpretation of the same.

The patient should stop breathing in midinspiration, for the exposure. If the plate is taken at the height of inspiration the heart will be lengthened and narrowed; if at the height of expiration it will be widened and made more round. It will be seen that between these two extremes quite a margin exists.

The thoracic diameter will also vary with the phase of respiration.

However, if the above precautions will be observed the margin of error or of variability will be reduced to a minimum.

We found as the result of these calculations that the normal heart is usually less than half the greatest diameter of the thorax:

$$\frac{\text{Heart (transverse diameter)}}{\text{Thorax (transverse diameter)}} \quad 39 \text{ to } 50 \text{ per cent.}$$

The average was about 45 per cent.

Because of the possible variations previously described, a margin of safety of 2 per cent. above the upper limit was allowed.

We may summarize as follows: Anything over 50 per cent. was regarded as suspicious. If other evidence pointed against the existence of hypertrophy, values up to 52 per cent. were regarded as normal. However, 53 per cent. and over were considered definitely pathological.

In many of the long narrow-chested individuals with small, "drop" hearts the occurrence of valvular disease and coincident cardiac enlargement will often yield neither an evident increase in the actual nor the relative cardiac size above the standard diameters of normal hearts.

In fact, figures as low as 46 to 47 per cent. (cardiothoracic ratio) are quite common in spite of cardiac hypertrophy. This means that a heart may be absolutely small though hypertrophied. Although apparently paradoxical this fact rests on sufficient proof.

Hence in cardiac hypertrophy the relative size or the cardio-

thoracic ratio may or may not be increased. If it is, it indicates cardiac enlargement. If the ratio is not increased, cardiac hypertrophy cannot be ruled out. In such a case the diagnosis will have to rest on the study of the intrinsic diameters of the heart and the character of the murmur and the history.

It is evident, therefore, that the size of a hypertrophied heart will depend to a large extent on the type of heart and its size before the onset of the cardiac affection. Thus a small heart (Tropfen Herz) may, in spite of a severe aortic regurgation—which is so apt to produce cardiac enlargement—still remain smaller than the standard diameter for the average normal. The cardiothoracic ratio is very apt to be altered, however.

Incidentally I should like to call attention to the fact that the cardiothoracic ratio is of value in the recognition of a tubercular predisposition. This is based on the view of Brehmer,[3] who said that a small heart with too large lungs is an important element in the predisposition to phthisis.

Hence, when the cardiothoracic ratio is definitely under 45 per cent. it points in favor of tuberculosis in the presence of suspicious lung signs. The lower the percentage the greater the presumption.

SUMMARY. 1. The cardiothoracic ratio is based on the anatomical relationship that exists between the heart and its containing frame, the chest.

2. The method of obtaining this information is within the reach of the majority of practising physicians. In other words, wherever a roentgen-ray laboratory exists the facilities are sufficient for this work.

3. The method has been tried out on a sufficiently larger number of cases (some 500 or more) to warrant its practicability and usefulness in the estimation of cardiac size, particularly in cases of moderate or early enlargement.

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CLINICAL STUDIES IN CUTANEOUS ASPECTS OF TUBERCULOSIS.

III. THE THERAPEUTIC MANAGEMENT OF THE TUBERCULIDS, WITH SPECIAL REFERENCE TO THE EFFICIENCY OF ARSPHENAMINE.

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IN studies Nos. I and II, I have reviewed the types of purpura, erythema multiforme and erythema nodosum which have a clinical association with systemic tuberculosis, and the diagnostic and clinical aspects of the papulonecrotic tuberculids and erythema induratum. Both of these studies emphasized the interest to the general diagnostician and the internist of this group of cutaneous lesions, which, while not themselves tuberculous in histopathologic architecture, are practically invariably associated with visceral tuberculosis, probably as an expression of bacillary infarction by hematogenously distributed tubercle bacilli plus cutaneous allergy.

In this study, the final one of the series, it is proposed to give an account of the method developed for the treatment of the papulonecrotic and erythema induratum types of tuberculids on the service of the Section on Dermatology. The report is based on 20 patients treated in a series of 30 under observation. It is intended to give primary emphasis to the effect of arsphenamine on the lesions and on the constitutional condition of these patients. None the less, a fundamental conservatism must underlie such a report. The longest period of observation reported is twenty-four months, and in all the cases adjuncts to the arsphenamine treatment, in the form of constitutional measures, roentgen ray to visible tuberculous foci, etc., have been employed. The ease with which *post hoc* thinking may be indulged in under such circumstances is fully appreciated, and for that reason what follows is to be interpreted as a preliminary report, albeit some attempt at critical analysis of the various factors in the treatment regimé is made.

SUMMARY OF THE CLINICAL ASPECTS OF THE SERIES.

For a fuller study of the clinical aspects of the group of tuberculids herein discussed, reference should be had to the previous studies. By way of summary it may be said that of the 20 treated patients, 6 presented the tuberculid known as folliclis, 1 had acnitis, which is the papulonecrotic tuberculid of the face, 8 had papulonecrotic tuberculids involving the trunk, 8 presented lesions of erythema induratum on the legs, 3 had tuberculous erythema nodosum, in association with other tuberculids, and the condition was quiescent in 3.

Visceral Lesions. Ten of the 20 patients (50 per cent.) had demonstrable tuberculous lymphadenitis in situations that were at least in part accessible to local therapeutic measures such as roentgen rays and surgery. Of the remaining 10 patients, 8 were "occult" or obscure cases, exhibiting no recognizable physical signs, with the exception of one who showed evidence of tuberculous involvement of the right apex with a negative roentgenogram. Three patients had positive Wassermanns without adequate objective evidence of syphilis, a condition discussed in Study II of the series. Four of the 10 patients having tuberculous lymphadenitis showed suggestive or diagnostic roentgenographic signs of pulmonary tuberculosis.

All the patients belonged to a type of tuberculous subjects having a high native resistance to the infection. None of them was acutely febrile or rapidly progressive. Several were fat and florid and to all outward appearances in robust health, conforming thus to a type which is familiar in association with visceral tuberculosis. The remainder were of smaller stature and slighter build, exhibiting a moderate pallor with asthenia, and, with surprising frequency, arthralgias and myalgias of the type usually associated with pyogenic focal infection. Several of the patients had mild grades of anemia, with afternoon temperatures fluctuating between 99° and 99.6°. Cough, hemoptysis and night-sweats were notably absent in the group as a whole. Loss of weight had occurred in a number of instances. In the overwhelming majority the cutaneous tuberculid was chronic, showing little disposition to remission and almost none to total disappearance. The group was therefore a good one in which to employ new therapeutic methods, since the presumption was strongly against spontaneous remissions in the guise of therapeutic effects. A number of the patients have shown the characteristic tendency to spring exacerbation, and several of these have now been carried through one and even two such periods without remission.

SPECIAL TREATMENT OF THE TUBERCULOUS FOCUS IN ITS RELATION TO A TUBERCULID.

The surgical work of the clinic has provided the opportunity to study, in connection with our work, the value of the surgical treatment of a tuberculous focus as a means of influencing a tuberculid. In estimating the effect of surgical extirpations of glands, however, it must be recalled that, as conventionally performed, such measures fall short of complete extirpation of the focus, and that results which such incomplete procedures fail to achieve can hardly be laid at the door of adequate surgery. On the other hand, the popularity of surgical treatment for axillary and cervical tuberculous adenitis justifies an estimate of the gross operative outlook when compared

with a proposed medical procedure for accomplishing a similar purpose.

A survey of 100 cases of tuberculous glands undertaken as a preliminary indicated that 37 per cent. of the patients had sustained one operation, 26 per cent., had been operated on twice, and 37 per cent. had been operated on more than twice. The highest number of operations sustained by any one patient was eight. The frequency of repetition noted must, of course, be ascribed, in part, to the impossibility or inadvisability in certain cases of attempting to extirpate a focus by a single procedure, and also, of course, to the inadequacy of the technic employed in some cases. None the less, the figures are suggestive in the light of our findings in patients with tuberculids. Nine of a total of 30 patients had received operative treatment in the form of excisions of glands for tuberculous adenitis. Three had had one operation with relapse; 2 had had two operations with indeterminate results; 3 had had two operations with relapse and 1 had had three operations and relapsed. Surgery had not, therefore, as applied in these cases, been conspicuously successful in eliminating the focus. In its relation to the tuberculid the following facts appeared:

The cutaneous outbreak had followed the operation in 4 cases, 3 after the first operation and 1 after the second. Operation had no effect whatever in 5 cases. In 1 of these one operation had failed, in the other three operations had been done without effect on the tuberculid. In 1 case constitutional benefit was reported, but the tuberculid persisted.

While due allowance must be made for the smallness of this group of cases, and for the unfairness of expecting one operation to accomplish what three may be necessary for, this much may be said to appear tentatively from our examination: Surgical treatment of a tuberculous focus as ordinarily carried out neither guarantees a patient against a subsequent tuberculid nor offers him any worthwhile therapeutic prospect if one is already present.

It should be recalled, in considering this point, that the best available pathologic and experimental evidence points to the belief that a tuberculid means hematogenously distributed tubercle bacilli from an active focus. Its occurrence after operation is, therefore, evidence for clinician and surgeon alike, that operative effort to extirpate the focus has failed. The repeated failure of operation to cure the condition simply registers repeated failure to get at the active process. A number of patients with tuberculids do not exhibit gross foci susceptible of surgical treatment. Forty-four per cent. of our patients showed no focus susceptible of surgical treatment. In such instances retroperitoneal and tracheobronchial tuberculosis and signs suggestive of localized tuberculosis in the abdominal cavity offer a plausible explanation, occasionally demonstrable at necropsy or by roentgenographic signs. It seems reasonable to believe that even in

cases in which there is a grossly obvious focus, such obscure and unreachable accessory foci may also exist. The failure of operation, when reasonably complete, to influence the course of a tuberculid should, therefore, it would seem, be interpreted as a signal to desist and to adopt in the place of further surgical intervention, measures to combat the focus constitutionally, by increasing the patient's resistance and affecting the walling off of the focus by physiologic means. Only a long series of cases can demonstrate, of course, that the medical procedure should have been invoked in the first place and the surgical procedure subordinated to it.

MISCELLANEOUS OBSERVATIONS ON TUBERCULIN TREATMENT, ETC.

The patients treated in this series offered opportunity for incidental observation of the effect or lack of effect of a miscellaneous variety of treatment. Of 5 patients with tuberculids, treated with tuberculin, dosage and method of employment unknown, 2 reported themselves as having been made much worse, following violent reactions. One had observed no effect, in another the glands had subsided (cervical lymphadenitis) without affecting the tuberculid, the fifth reported herself improved. I myself have observed the tendency to marked and unfavorable reaction to tuberculin sometimes exhibited by this type of case, with rapid extension of the process and believe that it may be aligned with the hypersensitiveness exhibited by cases of acute disseminating lupus erythematosus, in which reports of fatal outcomes are on record following the administration of small doses of tuberculin (Ravogli). MacKee has recently reported indifferent results in the treatment of a number of cases of the papulonecrotic tuberculid with tuberculin.

Three patients had received vaccines, 2 autogenous and 1 stock, presumably on a diagnosis of acne vulgaris or a pyogenic process. A patient with acnitis was made much worse, 2 others were improved, 1 of them a case of long standing. In an allergic complex such as that which underlies the development of tuberculids, it is difficult to determine the *rationale* of such a procedure, though it is conceivable that the improvement may be due to an action on the secondary focus of pyogenic infection present in more than 50 per cent. of these patients, as discussed in Study II. In both the patients who improved, such foci were present; the one had very septic tonsils and the other alveolar abscesses. This aspect of the therapeusis of tuberculids as well as their pathogenesis deserves further study. The effect of a vaccine, like the probable effect of arsphenamine, may be that of a non-specific stimulation of immunity and of defensive processes rather than a specific action upon the causal agent. One patient had received roentgen therapy to the lesions themselves. She reported that the ordinary dosages and methods were without

effect, but that one "deep" treatment had been beneficial. The *rationale* of this procedure is also doubtful, in view of the pathology of the tuberculid. It is possible that the constitutional effect of intense roentgen treatment accounts for the observed improvement.

Arsenic in other forms than as arsphenamine had been administered to three patients. One had taken enough Fowler's solution to produce palmar keratoses and hyperpigmentation, with little effect on the tuberculid. Another had received no benefit from the same preparation. One patient had received sodium cacodylate for anemia, with fair effect on the tuberculid. Her cutaneous lesions were subsequently cleared up by arsphenamine.

Mercury was intensively administered to 5 patients on the finding of a positive Wassermann. Three of them showed a normal tolerance of the drug by inunction or injection. The other 2 were less favorably affected. One of them was improved by iodides. Four of them noted improvement under arsphenamine. One patient had received iron for the anemia which marked the onset of active glandular tuberculosis, with marked benefit.

Local measures used in the cases observed were of little avail. A surprising amount of meddlesome surgery had been done on some of the lesions, notably when occurring on the leg, even to the point of repeated total excisions of lesions and deep incisions for supposed osteomyelitis, which had so damaged the blood supply of the tissues that satisfactory results could not subsequently be obtained.

Arsphenamine and Arsenical Synthetics in the Treatment of Tuberculids. The employment of arsenic in a variety of forms in the therapy of cutaneous tuberculosis has, of course, been familiar practice for a number of years. On the other hand, little of conspicuous benefit has been reported from it except perhaps in the sarcoids, a group of supposed tuberculids still of unsettled pathogenesis. With the advent of a new and highly potent arsenical in the form of salvarsan, an immediate attempt was made to apply it to the therapy of cutaneous tuberculosis. Herxheimer and Altmann, for example, early reported favorable results from its employment and asserted that they observed local reactions from its use similar to those obtained by tuberculin. While this latter observation has not been generally confirmed, other favorable therapeutic reports appeared. Just before the war Ravaut, followed by Tzanck and Pelbois, published accounts of marked benefit to a number of types of lesions of tuberculous origin from courses of salvarsan averaging three to six injections in number. The latter authors also urged the importance of an appropriate hygiene in the management of these cases. Sequeira noted the improvement of lupus vulgaris under atoxyl and salvarsan after mercury and the iodides, previously administered, had failed. The effect of arsphenamine on tuberculous subjects had been experimentally studied by Nicolas, Courmont and Gaté in 1912 and by Courmont and Durand in 1913.

These authors found that in experimental animals a marked increase in agglutinins for tubercle bacilli occurred in the blood on the administration of arsphenamine. Nicolas, Courmont and Charlet found a similar phenomenon to occur in the blood of tuberculous patients, and established at the same time that the increase occurs in those in whom the agglutinins are already high or on the increase rather than in those in whom they are low. In a therapeutic series of pulmonary cases in which novarsenobenzol Billon was given in small doses per rectum at frequent intervals, these authors felt their impression based on experiments, to be confirmed. They concluded that the drug should not be used in progressive or grave cases, which are aggravated by it, but in discrete limited involvements having a tendency to favorable course. The action was compared to that of sodium arsenite and arsphenamine rated as a reinforcement in selected cases. Potter, in summarizing his experience with 21 cases of combined tuberculosis and syphilis, reports favorably on the effect of arsphenamine, but cautious against its use in active, acute and miliary cases. He also noted the occurrence of tuberculin-like focal reactions.

My own experience with arsphenamine as represented by the types of tuberculous involvement included in the present series of cases is in accord with that of the authors mentioned. The effect of the drug does not suggest that of a specific bactericidal agent, but rather that of a fortifier of individual resistance and a means of stimulating the defensive mechanism of the body against the tubercle bacillus. Clinical study does not, of course, establish whether this is accomplished by the increased formation of specific agglutinins as suggested by the work of Nicolas and his collaborators, or by a less specific modification of the allergic and metabolic balance of the patient. My own observations in the use of arsphenamine in double infections with tuberculosis and syphilis accord with that of Potter in opposing the use of the drug in acute or unfavorably progressing cases or in those showing evidence of low resistance. One of the two conspicuous failures in our tuberculid therapeutic series was likewise a case of low resistance, running a rapidly progressive course. The patient died eight months after she was first seen. The ideal type for the use of arsphenamine, so far as our observations thus far suggest, is the patient who, while perhaps not on the up grade, is at least holding his own, who has seasonal periods when his resistance for the time being suppresses or controls all manifestations of the infection, and who rallies from the exacerbations produced by intercurrent ailments without a permanent break in his recuperative powers. The effect of arsphenamine in hastening the healing of ulcerative tuberculids, while not so striking as that in syphilomas, is none the less marked enough to suggest a degree of special action by this drug on granulomatous tissue, comparable to that exerted by potassium iodid, for example. This type of effect

may be similar to the effect of arsphenamine on blastomycosis, and, in my own experience, to the effect on occasional cases of sporotrichosis.

THE ARSPHENAMINE COMBINED TREATMENT OF TUBERCULIDS.

The use of this somewhat bizarre phrase is intended to imply that the regimé actually employed at the present time on the service of the Section on Dermatology in the Mayo Clinic is a combination of several therapeutic methods, including: (1) The intravenous administration of arsphenamine or neoarsphenamine, (2) the roentgen ray to detectable and accessible foci of glandular tuberculosis, (3) an antituberculous outdoor regimé, (4) a forced diet, (5) the removal of secondary foci of pyogenic infection in tonsils, teeth or elsewhere, and (6) the correction of vascular stasis and vasomotor abnormalities involving the extremities. Two items usually emphasized in texts we have found to be of secondary importance, that is, rest and local treatment of the lesions. It has been our experience that the former while of value need not be carried to the point of rest in bed with elevation of the affected leg.

The Arsphenamine Treatment of Tuberculids. Our preference in the selection of the preparation of arsphenamine is for arsenobenzol Polyclinic (Schamberg), although we have occasionally employed novarsenobenzol (Billon). The rather marked tendency to reaction exhibited by these patients has led us to prefer the former because of its exceedingly low toxicity and because of the same tendency to a lower intrinsic toxicity of the dihydrochlorate as compared with the monomethylene sulphoxylate of sodium salt which is observed in syphilis. The drug is given in courses, with a view to taking advantage of its cumulative effect. The average course is six injections, though later courses may be shortened. The dosage must draw a compromise between a maximum introduction of arsenic and the avoidance of toxic and debilitating effects from overdosage. The initial dose should not exceed 3 decigrams, the average dose 4 to 5 decigrams of arsphenamine or its neoarsphenamine equivalent. The injections should be given at weekly intervals. For the first 2 or 3 patients of our series, and for 1 seen subsequently but treated elsewhere, the dosage was small and the treatment desultory and irregular, to which we ascribe much of the relatively unsatisfactory results. The method should not be adjudged inefficient or inapplicable to a particular case until it has had systematic and persevering application.

At this stage in our employment of arsphenamine I feel it important to emphasize the repetition of the course as a seasonal reinforcement of the patient in the months of the year in which the tendency to relapse is usually greatest, that is, in March and November. In our series of 17 active cases, 4 patients received short courses of

four or five injections each, 6 have received thus far one course of six injections each, 3 received initial courses of eight injections. Three received two courses, totalling from eight to ten injections. Two received three courses, totalling ten and sixteen injections, respectively. One patient has received five courses, totalling twenty-four injections. The improvement exhibited by a given case is only incidentally a function of the number of courses. By estimating the total dosage in terms of grams of arsphenamine there is apparent, however, a relation between the total dose and the degree of improvement. Of 5 cases in which the improvement was rated as 4 on a scale of 0, 1, 2, 3, 4, the average dose was 3.8 gm. This omits from consideration 1 of our most remarkable cases, which was transformed by a total dosage of 10.8 gm., too high to be fairly compared with the other 5. Of the remaining cases, in which the patients showed improvements ranging from 0 to 3 and averaging 2 plus on the same scale, the average total dosage was 2.6 gm., or 1.2 gm. less than the dosage of the 4 class.

Improvement under treatment must be considered under three heads: (1) improvement in the cutaneous lesions of the tuberculid, (2) improvement in the constitutional condition of the patient, and (3) improvement in the tuberculous focus if observation of it is possible.

The improvement effected in the tuberculid by the administration of arsphenamine is often the first change apparent under treatment. Usually with the first and second injections, but sometimes not until the fourth, there are marked drying and reduction in the size of any active lesions present and a diminution in tenderness. The course of any new lesions which may appear is markedly shortened and the number of recurrences greatly decreased. In a case which is progressing favorably, new lesions have ceased to form by the end of the first course, although even in cases which ultimately remain clear there may be slight relapses. In several of the cases in our series which were at first rated as failures the patients have recently reported that they consider themselves much improved, owing to the fact that although lesions still appear they have practically ceased to be troublesome.

The treatment results in our series may be summarized from the standpoint of cutaneous lesions as follows: Of 17 patients presenting active lesions, 9 (53 per cent.) have been completely cleared of active lesions, 5 in the first course, 3 in the second and 1 later. Four patients have been improved though not protected from relapse; treatment of these is incomplete. Four cases of the series (24 per cent.) were rated as failures before the sending out of a questionnaire while the present study was in preparation. As a result of this questionnaire it appears that one of the "failures" rates herself as 50 per cent. better than before treatment. She still has nodular recurrences but no ulcers. Her total dosage was 4.1 gm. in ten

injections. The second "failure" reports herself as "a great deal better," and as having gained 40 pounds in weight, although she is again down to medium weight. This was one of our early patients who received unsystematic treatment with rest in bed. The outlook for complete symptomatic recovery was greatly reduced by the amount of surgical trauma inflicted on the legs, which were the sites of most of the lesions. Numerous incisions, excisions and attempts at plastic treatment of the ulcers had practically ringed the affected area about with scar-tissue, creating an artificial stasis. The two *bona fide* failures were a woman with an erythema induratum of the calf of one leg and a tuberculosis verrucosa cutis of the other, with a progressive anemia and asthenia. While no active focus could be identified, she was reported dead in response to a questionnaire. The second failure was in a rather obese woman, a low resistance type, with innumerable scars of suppurating cervical glands and a history suggestive of tuberculous peritonitis with a focus in the adnexa. She had an inadequate early course with overattention to local measures, and relapsed the following spring, with more suppurating glands. If in 2 of the 4 cases described the patients may be rated on their own estimate as improved, the percentage of total failure to improve the cutaneous condition will be reduced to about 12 per cent.

Precisely how much of the constitutional improvement manifested in these patients is to be attributed to the arsphenamine which they receive it is difficult to say. Undoubtedly the storage of arsenic in the liver and spleen which occurs during a course of injections provides the basis for a prolonged tonic effect. On the other hand, a number of our patients showed definite improvement in their general symptoms while receiving the first course of injections, and this in face of the fact that they were not encouraged to adopt any special hygienic measure until the interim between courses, and again in spite of the fact that some of them resumed hard work which they had been physically unequal to prior to beginning their course of injections.

Gain in weight and an improvement in or complete disappearance of "rheumatic" symptoms if present were the two most immediate and conspicuous effects on the general health of the patients. The weight gains during the course of treatment varied from 1.5 to 13.5 pounds. The tendency to gain weight continues to manifest itself after the completion of the course, and in fact many of the most striking increases occurred in the month following the arsphenamine treatment, a phenomenon we have repeatedly observed in the treatment of syphilis. While the weight changes are undoubtedly to some extent influenced by forced diet and hygiene, the changes occurring under arsphenamine alone are sufficiently marked to make it probable that the drug was largely instrumental in the improvement.

Of 14 patients on whom definite data are available, not one has failed to register some gain in weight. Seven (50 per cent.) have

FIG. 1.—Acnitis, the papulo-necrotic tuberculid of the face. Scar of operation for tuberculous adenitis visible on the neck. The eruption followed the operation. Photograph taken before arsphenamine treatment was begun.

FIG. 2.—After five injections of arsphenamine—only scars and pigment macules remain.

made gains varying from 7.5 to 40 pounds in periods varying from two to twenty-four months. Four patients gained more than 20 pounds. While the peak of the weight curve is not always maintained, 4 have held gains of 15 pounds or more for from one to two years.

Loss of weight may occur, especially in the obese. Three patients lost from 7 to 10 pounds during their course of arsphenamine injections. This was accompanied by an increased sense of well-being rather than the reverse.

FIG. 3.—Four months later after three more injections of arsphenamine. Complexion clear and blooming.

The effect of arsphenamine on the arthralgias and vague aching pains which many of these patients present is often very striking. A patient who had been operated on for a tenosynovitis without improvement, and who had multiple swollen and painful joints (both ankles and the right knee), was completely relieved of her symptoms by the fourth injection of her first course and has suffered no recurrence. Another, at one time bed-ridden for weeks with "rheumatism," has had no such symptoms since her first course, and only notices a slight aching when extremely fatigued. A barber who registered the maximum weight gain under treatment remarked enthusiastically that he had gone back to earning a living after having been unable to be on his feet for more than an hour a day for two years on account of pain and swelling of the ankles.

While our observations are still too few in number to permit of

generalizations, we have not been impressed with any marked influence of the arsphenamine on the tuberculous adenitis insofar

FIG. 4.—Lesions of follicles before the administration of arsphenamine.

FIG. 5.—Same case as Fig. 4. Lesions healed following six intravenous injections of arsphenamine. No other treatment used.

as it can be judged by a reduction in the size of the glands. In 2 cases actual increase in the size of the glands seemed to occur during the early part of the course, and a rapid reduction subsequently followed

the first one or two Coolidge tube exposures. In other cases the glands were very little influenced. Several patients in response to a questionnaire, report reductions in the size of the palpable glands, but such reductions occur so often as a result of improved hygiene and a period of freedom from secondary infections that no conclusions can be drawn.

About 50 per cent. of patients with tuberculids seem to exhibit a distinct idiosyncrasy for arsphenamine, a figure very much in excess of the average reactivity displayed by syphilitics for a similar dosage and interval scale. Of 9 patients, 4 had single or repeated nitritoid crises, 4 had pronounced gastro-intestinal reactions and 1 developed a toxic erythema, a very rare accident on our service. As in the treatment of syphilis, a definite overtreatment syndrome with marked idiosyncrasy, loss of weight, pallor and nervousness is an indication for abandoning arsphenamine.

Roentgen Therapy. Our experience with the roentgen ray in the treatment of tuberculids has been largely confined to its use in treating a glandular focus. The earlier technic employed was less efficient than the later, and for that reason no final conclusions are possible. The treatment recently given under the direction of Dr. Jones in the Department of Roentgenology of the Mayo Clinic has consisted of a four and one-half minute exposure with the Coolidge tube on a 4-inch square surface over various parts of the mass, using a current of 5 ma. with a 7- to 9-inch spark gap and a focal skin distance of 9 inches. The filter employed has consisted of 3 mm. of aluminum, 1 cm. of wood and 5 mm. of sole leather. With this technic we have seen a definite effect on glands which we did not believe could be attributed to any other factor in the treatment.

On the other hand, the effect of roentgen treatment of the glands on the tuberculid seems to us more open to question, especially when compared with that of arsphenamine. One patient who improved slightly under *x*-ray alone registered the most surprising gains under arsphenamine at a considerably later period when the ray had been discontinued and its effects must have worn off. A second patient received *x*-ray to the glands at intervals without effect on the tuberculid or the glands, but the tuberculid improved subsequently under arsphenamine. In a third patient the lesions were cleared up by arsphenamine and no *x*-ray was employed until later. Three of six patients presenting a glandular focus made remarkable gains without any *x*-ray, and in several occult cases in which the patient presented no indication for its use, remarkable improvements were likewise made. While roentgen-ray treatment of the focus of tuberculous infection in a glandular case has its function, it cannot be regarded either as a substitute for arsphenamine in the control of the tuberculid or as comparing with it for promptness and of efficiency in the cases under our observation.

Outdoor Regimé, Forced Diet and Rest. Since it is axiomatic that the treatment of a tuberculid is that of the underlying tuberculosis, emphasis has been placed with the patient on these means of cultivating an increased resistance. That their part is to increase the permanence rather than the striking quality of a therapeutic result is the impression derived from observation of those of our series who have adopted our recommendations. A number of patients have made and held marked improvements without giving this aspect of their treatment the attention it deserves. On the other hand, the four or five patients who have been longest under observation and give the greatest promise of permanence have at least slept outdoors, even though following indoor occupations, and have conformed to the general principles of antituberculosis hygiene. Rest, particularly in bed, has not been urged on our patients at any stage, and we have noted distinctly inferior results in our earlier cases when the patients were confined in order to secure the effect of rest on the lesions. Several patients have had notable results while pursuing strenuous occupations, such as housework sixteen hours a day, barbering and heavy teaming.

Treatment of the Secondary Focus of Pyogenic Infection. As shown in Study II, a high percentage of patients exhibiting cutaneous tuberculids have a secondary focus of pyogenic infection in the form of septic tonsils, alveolar abscesses and possibly, in some cases, foci, such as infected gall-bladders, etc. When such a focus could be identified we have found it advisable to remove it, although its precise role in the production of the tuberculid is undetermined. Such a removal is not sufficient in itself to cause the disappearance of a tuberculid without appropriate general measures and special treatment directed at the tuberculous focus if it can be identified. We observed in one case, however, that a single obstinate and persistent lesion on the leg which had refused to yield to the regimé which had cleared up all the others, healed after the removal of markedly septic tonsils. On the other hand, in several of our patients the tuberculid appeared at varying intervals following tonsillectomy.

Correction of Vascular Stasis. The value of the elastic bandage in hastening the involution of papulonecrotic lesions on the legs even in the absence of gross vascular abnormalities, such as varicose veins, was early apparent, and did much to keep our patients out of doors and active. In cases exhibiting vasomotor anomalies, as in the thinner and more neurotic types of patients, two pairs of stockings, silk and wool, or specially warm clothing and gloves, were of value in improving the peripheral circulation and diminishing the severity of recurrences.

Miscellaneous General Observations. Taken as a group, the least favorable results are to be expected from the obese, florid types of patients. The majority of them have erythema induratum, and the marked stasis element in the blood supply to the leg seems

to predispose them to recurrence, although the temporary therapeutic response of a group of lesions may be good. Seventy-two per cent. of the patients having an occult or obscure focus of tuberculosis were in the less successful group as regards therapeutic results, while only 28 per cent. of patients of this type make a maximum improvement. When anemia is a prominent feature the internal administration of iron is necessary to secure a marked rise in hemoglobin, the arsphenamine having proved less efficient in this regard.

CASE HISTORIES ILLUSTRATING THE TREATMENT DESCRIBED.

CASE 1 (161592).—A girl, aged nineteen years, had been the victim of severe and extensive papulonecrotic lesions with erythema induratum since the age of nine years, associated with a severe tuberculous adenitis and with tuberculous keratitis and severe anemia. Under twenty-four injections of arsphenamine, totalling 10.8 gm., the patient has gained 28 pounds in weight and held it and is practically free of lesions. She had pursued exacting indoor occupation for one and one-half years, and is in excellent general health. She has had one abortive attack of episcleritis since being under observation, but has shown no other manifestations of tuberculosis. Period of observation, two years.

CASE 2 (174923).—A girl, aged twenty-four years, unsuccessfully operated on for tuberculous glands, has had a long history of severe papulonecrotic lesions on the buttocks, thighs and legs and arthritic and myalgic symptoms of such severity as to confine her to bed for weeks at a time. Under sixteen injections of arsphenamine, totalling 6.0 gm., combined with an outdoor regime and nine Coolidge tube exposures, she has gained 20 pounds in weight, maintained it for twenty-two months, has never had a lesion since the first course and now does general housework at home, whereas before treatment she was a semi-invalid.

CASE 3 (200833).—A nurse, aged thirty years, who had been operated on twice for tuberculous cervical adenitis, with only partial success, had a profuse acnitis of the face and ears and a papulonecrotic tuberculid of the forearms. She had received vaccines for acne which made her worse. The eruption vanished before the completion of a five-injection course and at the end of a second additional course of three injections, with a total dosage of 2.6 gm., her complexion was blooming. Her reply to a recent questionnaire states that she has followed only a partial outdoor regimé, has gained 7.5 pounds, of which she has held 3 pounds, feels well, has never had a relapse, the glands are palpable and about stationary and she is contemplating Red Cross work.

CASE 4 (212370).—A girl, aged twenty-five years, had been seen by numerous internists and surgeons without a diagnosis having been made. She presented a typical folliclis, with an erythema induratum and papulonecrotic tuberculid. In addition she had a tenosynovitis which had been unsuccessfully operated on and a slight hydrarthrosis of both the ankle and right knee, with marked arthralgic and myalgic pains. A tonsillectomy and appendectomy previously performed had been without effect on the trouble. Ten injections of arsphenamine with an outdoor regimé between the two courses resulted in a net gain of 14 pounds in weight, and the total disappearance of all symptoms and signs, including the eruption, the tenosynovitis and the hydrarthrosis by the end of the second course. The patient has been under observation for ten months.

CASE 5 (226884).—A man, aged forty-two years, a barber, who had been unable to work for two years, had an extensive papulonecrotic tuberculid of the legs and trunk and enlarged cervical glands. Under a first course of eight injections of arsphenamine, totalling 3.4 gm., he gained 13.5 pounds in weight, returned to full-time work and has followed no special hygiene. He has subsequently gained an additional 7 pounds. Roentgen ray was not begun until the end of the course, so that the effect must be attributed entirely to the arsphenamine. All cutaneous lesions have disappeared. The glands, while smaller, are still present.

CASE 6 (218528).—An anemic but well-nourished woman, aged twenty-six years, who had lost 40 pounds in weight in four years, presented a papulonecrotic tuberculid of the leg of eighteen months' duration with erythema induratum and a mild secondary anemia without obvious signs of tuberculosis. Under a single course of six injections, totalling 2.4 gm. of arsphenamine, she reports after nine months a gain of 17 pounds in weight and the "wonderful" disappearance of her lesions without signs of recurrence.

CASE 7 (197425).—A girl, aged twenty-one years, of the overweight, florid and blooming type, presented the ulcerative lesions of erythema induratum on both legs, with numerous nodules. She received ten injections of arsphenamine, with a total dosage of 4.1 gm., doing heavy housework sixteen hours a day during the treatment without any special hygiene other than the use of elastic bandages. All the ulcerative lesions disappeared, but nodules occasionally recurred. At the end of fourteen months, in reply to a questionnaire, she reports an improvement of 50 per cent. The lesions are smaller, fewer and less painful than before treatment and last only about a week. She is doing indoor work and sleeps out of doors.

It will be apparent from the discussion and the cases cited that final judgment cannot at this time be passed on the use of arsphenamine either alone or in conjunction with other measures in the management of tuberculids of the papulonecrotic and erythema

induratum types. Only time can establish the permanence of the results. On the other hand, there seems good reason to believe that it has a marked beneficial effect proportional to some extent to the persistence with which it is used and to the total dosage of arsphenamine administered. Some of the results produced in the patients longest under observation and treatment have been really remarkable, and failure and lack of improvement can, in a number of instances, be explained by desultory methods. In general, the obese types of patients, and those with occult tuberculosis, offer less outlook for radical improvement than other types, but it is impossible at the present time to generalize or to predict in which case improvement may or may not be expected. When the long duration and the persistence of tuberculids of this type and the heretofore rather dubious results of conventional methods are taken into consideration, I believe the intensive use of arsphenamine in conjunction with a regimé which treats the underlying cause as well as the symptom deserves to be better known and more extensively employed.

SUMMARY.

1. This study deals with a group of 20 cases of various types of papulonecrotic tuberculid and erythema induratum in which arsphenamine (Ehrlich "606") was used with good effect in combination with a systemic regimé and roentgen therapy.

2. Over half the cases thus treated had demonstrable tuberculosis, usually in the form of a lymphadenitis.

3. Surgical treatment of the lymphadenitis in 9 cases had not demonstrably affected the tuberculid.

4. It would seem from our series that the appearance or the persistence of a cutaneous tuberculid following reasonably complete surgery is an indication for a discontinuance of surgical treatment of the tuberculous focus, and the adoption of a medical means of fortifying the patient against the progress or recurrence of his tuberculous infection.

5. The intravenous administration of arsphenamine would seem to afford such a medical means of fortifying the patient's resistance to tuberculosis when combined with an antituberculous hygiene and roentgen ray.

6. Arsphenamine offers an excellent means of treating selected cases of obscure tuberculosis as evidenced by the presence of a tuberculid in the absence of a demonstrable focus. Its use in febrile, acute or rapidly progressive cases is not advised.

7. Arsphenamine alone is apparently able to produce a striking effect on cutaneous tuberculids. Fifty-three per cent. of 17 cases have been completely cleared of lesions and only 12 per cent. have failed to secure a definite improvement.

8. Arsphenamine is also apparently instrumental in producing a marked constitutional improvement in these cases, evidenced especially by a gain in weight and the disappearance of the "rheumatic" symptoms complained of. Gains of from 1½ to 40 pounds were registered in our series.

9. The effect of arsphenamine upon the tuberculous adenitis where present is indeterminate, but probably not striking.

10. Roentgenotherapy assists in the reduction of the glands, but we have not found it to compare with arsphenamine in its influence on the general condition or on the cutaneous tuberculid.

11. An outdoor life, forced diet, correction of vascular abnormalities and stasis by elastic support, and careful extirpation of secondary foci of pyogenic infection in tonsils, teeth, etc., are subsidiary but important elements in a successful treatment.

12. These observations are offered as tentative and preliminary, although several of our cases are completing their second year of freedom from lesions and striking general improvement.

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THE PREVALENCE OF TRICHOMYCES INFECTIONS IN WESTERN NEW YORK, WITH SPECIAL REFERENCE TO B. FUSIFORMIS.

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During the past eighteen months routine bacteriological findings, including B. fusiformis and spirillary filaments, have been so frequent in this locality that I feel justified in making a general report of their clinical distribution, although some of the cases are sufficiently unique to merit separate communications, and for this reason only their salient features will be presented at this time. It is certain that during this period I have encountered such cases with a markedly greater frequency than experienced during a seven-year stay in the University of Michigan. Dr. Lloyd,[1] Medical Director of the Monroe County, N. Y., Sanitarium for Tuberculosis, has over a similar period noted more cases of chronic non-tuberculous pulmonary infection than he has encountered in a number of years' experience in other localities.

Whether their prevalence is representative of conditions in this country cannot be said with certainty at present. The fact that Barker and Miller's[2] paper on the subject is one of the few I have encountered may only mean that other observers have not considered the subject as important. From military sources abroad, however, numerous reports of a high percentage of Vincent's angina cases have appeared, as instanced by the work of Campbell and Dyas,[3] McKinstry,[4] Bouty,[5] Bowman[6] and others quoted by the first-named authors. Perhaps these findings have not extended over a sufficient space of time to designate them as fairly representative, although there is evidence that some organisms of the trichomyces group—notably actinomyces—are particularly common in the soil of western New York.[7] The well-known predilection of the blastomyces and sporothrix infections for the Missouri Valley may be to an extent comparable with the presence of certain members of the trichomyces group in this locality.

The constant association of B. fusiformis and spirochetes as the predominating organisms in noma, ulcerative stomatitis, pulmonary

[1] Personal communication.
[2] Jour. Am. Med. Assn., September 7, 1918, p. 793.
[3] Jour. Am. Med. Assn., June 2, 1917, p. 1596.
[4] Practitioner, London, 1917, xcix, 507.
[5] British Med. Jour., 1917, ii, 685.
[6] Proc. Roy. Soc. Med., 1915, ix, Part 2, p. 51; Lancet, London, 1917, ii, 536; British Med. Jour., 1916, i, 373.
[7] Conn, H. J.: Agricultural Experiment Station, Geneva, N. Y., personal communication.

gangrene, putrid bronchitis, gangrenous balanitis, etc., has served to give them etiological significance, although this relationship as well as many points in the biology of these organisms cannot as yet be said to be categorically established, owing chiefly to the rather uniform failure of pure cultures to reproduce the conditions in experimental animals. This phase of the subject which has yielded certain conditional results will not be discussed in this paper.

My attention was first directed to these organisms by a case of generalized streptothricotic infection. One of the commonest conditions encountered has been chronic bronchitis, which frequently was associated with such a foul odor as to merit the designation of putrid bronchitis. Almost invariably these cases have been considered tubercular, owing principally to the duration of the cough, which is usually a matter of several weeks or months, although in one case there is good reason to believe it has existed for fifteen years, covering almost the entire lifetime of the patient. The sputum is usually mucopurulent, and in some of the older cases lymphocytes predominate. Although in certain of the cases, particularly the more acute ones, no difficulty is experienced in finding the organisms, in others they are often restricted to little opaque spherules or grayish-white flakes, which may represent practically pure colonies. In the absence of the tubercle bacillus, assiduous search should be made for these flakes or spherules. They are comparable with the sulphur granules of actinomycotic pus and the caseous masses of tuberculosis, although their consistency is by no means cheesy. From a total of 60 cases, constituting 9 per cent. of our bacteriological examinations, 24, or 40 per cent., have been clinically confused with tuberculosis.

Case I.—This patient suffered from chronic bronchitis of fifteen years' standing, upon which bronchiectasis and pulmonary fibrosis were superimposed. It followed whooping-cough at two years of age, and some of the best authorities had failed to diagnose it as tuberculous. The sputum contained many of the flakes above mentioned, and when washed were seen to contain a pure culture of a non-acid-fast anaërobic organism, fusiform in shape and decidedly granular, resembling the beaded form of the tubercle bacillus. The patient had a blood count of 20,000 to 25,000 unless she remained relatively inactive. This case, a patient in the service of Dr. J. R. Williams, will later be reported in full.

Case II.—This case was one of extensive acute bilateral empyema, diagnosed as pneumonia. At autopsy the lungs were negative. The condition was of three weeks' duration, and the last week was characterized by the appearance of mental symptoms suggestive of cerebral involvement. The spinal fluid was very purulent, the condition being one of extensive meningo-encephalitis. The only other finding of note relates to the aortic opening of the heart, whose middle valve was the seat of a friable verrucose excrescence, the

size of a very large pea. Section of this nodule revealed mainly necrotic material, a Gram-Weigert stain of which disclosed myriads of coccoid forms of varying size, and short curved bacillary forms, many of which showed rudimentary branching. From the pus of both lungs and from the spinal fluid the same organism was isolated in pure culture.

Colonies on blood-agar were of medium size, semitransparent or translucent. Microscopically the elements were somewhat pleomorphic; coarse, loosely wavy spiral forms predominated. Vibrio forms were also present, some of which were slightly granular at the ends, while others were somewhat club-shaped and granular, resembling diphtheria bacilli. Great variation was noted in the diameter of the different curved forms, some being so slender as to simulate a loosely wavy spirochete. Rudimentary branching was observed. Such forms were found on direct examination of the spinal fluid also. Repeated plating did not show a mixed culture. When first isolated the culture had distinct anaërobic tendencies, but later grew aërobically.

There also occurred 1 case of unilateral empyema and 1 of an acute bronchopneumonia whose sputa were filled with colonies of B. fusiformis. Cases III and IV were pleural effusion, one acute and the other chronic. The acute case was of such sudden onset as to have the physical signs of a severe lobar pneumonia, but the characteristic mildness of the clinical symptoms decided the diagnosis in favor of effusion. After withdrawal of 3 quarts of fluid the patient made a rapid recovery. Although 20 c.c. of this fluid were injected into a young guinea-pig, the results were negative. The organism resembled in its general character the one isolated from the case of empyema.

Case Group V. There have been in all 8 cases of Vincent's angina, 6 of the pseudomembranous type and 2 of the ulcerative type. One of the latter has recurred at intervals of two and three months, respectively. Of 2 cases of ulcerative stomatitis, 1 was characterized by the presence of a single large indolent ulcer on the mandible behind the last left molar tooth. The other case was of twenty-five years' duration, characterized by the presence of crops of ulcers, located particularly on the under surface of the tongue and floor of the mouth, but to some extent on the buccal mucosa as well. Occurring in a physician, they came and went without warning and without power for control on his part, until he was finally forced to resign from active practice. The fusospirillary complex was found several times during the past ten years, but was always considered in the light of a secondary invasion. The condition was associated with gingivitis, and one particularly unsanitary crown was present. Removal of the tooth on which it was located revealed myriads of these organisms around its root, one fang of which had suffered necrosis to the extent of half its substance.

CASE GROUP VI.—There were 3 cases of chronic gingivitis, 1 in a boy, aged six years, from very good hygienic environment, was of interest. This child suffered from progressive loss of teeth. The mother said they simply dropped out, one by one, without apparent cause. The appearance of the gums was good, with the exception of a slight dusky hue. No exudate was visible, although a swab passed over the gums revealed rather numerous pus cells and large numbers of long wavy filaments, with a few fusiforms.

CASES VII and VIII.—I have observed 2 cases of pharyngeal and tonsillar mycosis (mycotic pharyngitis). Clinically these cases were characterized by the presence of whitish-yellow cone-shaped elevations attached to the mucosa of the tonsils and their crypts and the pharyngeal wall near the uvula. The adherent quality of these elevations was their most noteworthy characteristic, it being impossible to detach them even with an instrument. Histologically they were characterized by a hyperkeratosis of the mucosa, replacing all but its deepest layer. Between the lamellæ composing these nodules numerous bacillary filamentous forms and cocci were observed.

CASE IX.—This case was one of gangrenous balanitis, the so-called fourth venereal disease. It occurred in a man, aged fifty-five years, starting on the prepuce as a small pimple. From picking it and from irritation in other ways it soon increased in size, and later suppurated. The patient refrained from calling a physician for six months, despite what must have been an alarming increase in its size. When first observed the glans and adjacent body of the penis were about the size of an orange, and where the skin and mucosa were intact the color was very dusky red. A deep, gaping ulcer was eaten out of the swollen glans. The walls of this ulcer were ragged and overhanging, the one from the dorsal surface of the penis projecting in flap-like form, but partially constricted at its base by the phagedenic process. The entire ulcerous portion was deluged in a viscid purulent exudate of foul odor. Microscopically, in addition to numerous cellular elements were myriads of fusiform organisms and long, wavy, slender branching filaments, together with shorter and actively motile spirochetic forms. The blood-culture results will be detailed later. The Wassermann and the complement-fixation reaction for gonorrhea were negative.

CASE X.—This case showed a slow gangrene of the lower extremities, the symptoms taken, as a whole, suggesting Raynaud's disease. The patient gave a history of severe mouth infection four years previously, followed by exacerbations from time to time. The Wassermann reaction was repeatedly negative. Amputation of one leg disclosed a proliferative, obliterating endarteritis in the tibial vessels. Stained with Gram-Weigert there was no lack of pleomorphic, bacillary and coccoid forms positive to Gram, and filamentous and rudimentary branching forms, partially or totally

decolorized. The Levaditi stain for spirochetes was negative. I do not care to draw any conclusions in this case, but the demonstration of this type of organism in the lesions is of note when the pathology rules out Raynaud's disease and syphilis cannot be demonstrated.

CASE XI.—A boy, aged twelve years, developed a slowly progressive painless monarthritis of the knee-joint, with effusion. No growth was obtained either aërobically or anaërobically from this fluid, but direct examination of the sediment showed granular bacillary forms, some of curved fusiform shape; some coarse solidly staining filaments were also present. Certain of the coccoid forms gave rise to wavy filamentous structures.

Cultures of the tonsils and throat yielded, in addition to the usual cocci, large numbers of long, wavy filaments and diphtheroid forms. Some of the filaments undoubtedly arise from the ends of the diphtheroid or fusiform-like organisms and have a general conformity with those found in the exudate from the knee-joint. A tonsillectomy was followed by recovery of the patient, who has since remained well (six months). It should be noted, in addition, that intravenous injections of foreign protein formed a part of the treatment.

CASE XII.—Another case in point was one of Dupuytren's contracture of fifteen years' standing, which followed streptococcic sepsis from accidental wound infection. For the past five years a slowly progressive general adenitis had developed, and latterly symptoms suggestive of spondylitis. These consisted of spinal rigidity, with pain and tenderness over the spinal muscles and posterior nerve roots. A pure culture of a spirillum was isolated from the tonsillar crypts in practically pure culture, while only an occasional colony of the organism was present on the pharyngeal mucosa. Tonsillectomy in this case has resulted in the immediate disappearance of the spinal symptoms, but has had no effect as yet on the adenitis or the contracture. The patient has gained fifteen pounds in weight, and his capacity for work has been much increased.

CASE XIII.—This case was one of a tumor, slowly progressive in character, which developed in the abdominal wall. Pathological examination revealed a chronic infective granuloma suspiciously tuberculous. Although no specific tubercles or bacilli could be found, the granulomatous tissue was markedly endotheloid in character. The center was broken down, and among the dense, purulent infiltration of leukocytes were large numbers of eosinophiles. A Gram-Weigert stain showed the same type of organism previously described, but in this case the specimen was unfortunately fixed before we had opportunity for a culture of it.

Other cases showing similar findings are briefly: One mastoid abscess ending fatally, organisms recovered in purity (Case XIV) and several of postpartem fever (Case Group XV), in which no

organism could be found in the discharges, but which may have originated from a severe gingivitis, showing fusospirallary organisms (Vincent's), and will be further discussed in connection with the blood-culture results. Organisms of the type under consideration were recovered from one extremely interesting case of toxic hyperchromatic anemia simulating pernicious anemia, arising probably from intestinal ulcers (Case XVI) and a case of unilateral salpingitis, non-gonorrheal in origin (Case XVII).

Results of Blood Cultures. Although for the most part organisms of this character are not found in the blood, in 8 of the 60 cases blood cultures were positive. Cultures were taken in broth and not discarded before the end of ten days, inasmuch as the growth was often slow in appearing. In some cultures it was difficult to determine with certainty whether actual organisms were present, and their relation to the pathological conditions cannot be told with finality at present.

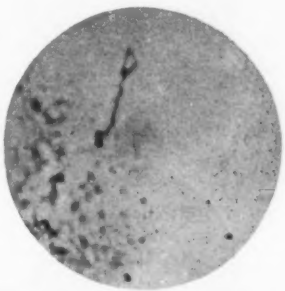

Fig. 1.—Filamentous form occurring in transplant from seventy-two-hour blood culture. In the adjacent triangular coccoid form there are three minute highly refringent areas, peripherally located. Many similar gonidia (?) are found free in the culture. Romanowsky. × 1000.

In the culture from a case of gangrenous balanitis a slowly increasing flocculent sediment appeared after three or four days. The best staining results were obtained with the Romanowsky. Cocci and coccoid forms varying greatly in size were found. Many of the cocci had one or more short projections which suggested that actual filaments might so arise. Prolonged search of this culture shows such to be the case (Figs. 1 and 2). In Fig. 1 the short coarser projection arises from a highly refringent area at the periphery of the coccus, which in turn gives off a more slender and somewhat wavy long filament, in the course of which is interpolated another coccus form. Note that the slender filament arises from the side of the coarse projection: (*a*) From the end of solidly staining filament three faintly staining loops arise. Under certain environmental conditions the filament itself may traverse these loops longitudinally, when

they might be considered as formations homologous to the clubs of the actinomyces.

In Fig. 2, about the middle of the filament, a small oval non-staining body, with fine terminal granules, is present. Similar highly refringent circular bodies, from one to three in number, are found in the cocci and coccoids as well as free in the smear. There is some evidence that they represent gonidia and have to do with the reproduction of the organism. Giant coccus forms, from 3 to 5 μ in diameter, can also be seen, some of which have several projections, which give them a stellate appearance (Figs. 4 and 5).

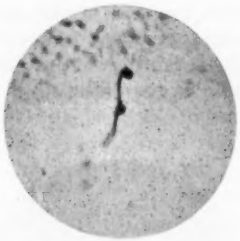

FIG. 2.—Note highly refringent oval body in the course of the filament. Romanowsky. × 1000.

FIG. 3.—Periplast formation developing about the filament, part of which is marginally located. From the depths of hormone agar. Carbol-fuchsin. × 1000.

It is of particular interest in this case that a suspension of these cocci (?) agglutinated the patient's serum in a 1 to 50 dilution, while a normal control in a 1 to 10 dilution was negative. In certain of the other cases, however, no immune reactions were obtained. These cocci may represent a stage in the life-cycle of a filamentous organism. However that may be, it is certain that a hasty examination of this culture would not have shown these filaments in their well-developed form, while their rudimentary form might have been viewed as an artefact. It is to be presumed, at least, that they were related to similar ones seen in the lesion.

In another type of blood culture this diplococcus form is not seen, or if seen, does not grow in transplants under the usual conditions.

In these cases large circular forms predominate, containing usually from two to five oval faintly staining bodies. They may have in addition one or more filamentous projections of varying length. In case the center of the cell is achromatic, the latter spring from well-defined granules located at the periphery of the cell. Cases I, V and XII and one of intermittent fever not discussed here were of this latter type, while the former were represented best by Cases IX, XI and XIV. Cases XVI and XVII were repeatedly negative, which is also true for the remainder of the cases discussed.

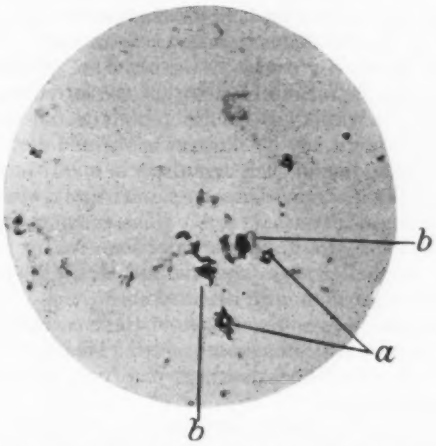

FIG. 4.—Giant coccus forms: (*a*) early, (*b*) late. Note development of filament from (*b*). From a twenty-four-hour hydrocele broth culture, thirty-fifth generation. Romanowsky. × 1000.

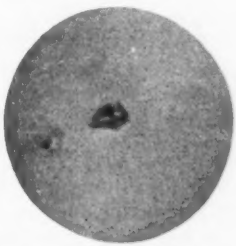

FIG. 5.—Another giant coccus form, with intracellular light areas and chromatin granules. Romanowsky. × 1500.

RESUMÉ. In this locality during the past year certain members of the trichomyces group of organisms have been found, with considerable frequency, particularly in pathological conditions of the upper respiratory tract. In certain instances the infection becomes generalized. The most prevalent type of case is a chronic bronchitis

which at times may be of long standing and which may closely simulate tuberculosis. Experimental work is in progress.

The pathological role of B. fusiformis and related organisms may be of greater significance than has been supposed. The results of the blood cultures, particularly in cases with positive immune reactions, is suggestive. The presence of filaments in the blood of cases having local infections of this sort must be accounted for and the condition of their growth is such that they may easily be overlooked. An experimental investigation of the bacteriology of one unreported case of undoubted generalized streptothricotic infection suggests that the various kinds of circular bodies found in the blood may be related to the filaments in a cyclic manner. It is probable that some of the cocci grown from the blood are secondary invaders, as it is becoming better established that the latter may invade the organism under a variety of conditions. It would seem, however, that the type shown in the illustrations would not come in this category. The finding of such organisms in mildly febrile puerperal cases in which local uterine signs are negative suggests that the susceptible pregnant state may permit their entrance into the blood from a distant focus of low-grade infection—as, for example, from the mouth. In the few cases we have had their disappearance from the blood was coincident with defervescence.

Metastatic foci may at times arise in these cases and isolation of the organisms in purity be accomplished. This fact, together with their apparent prevalence, does not justify us in regarding them solely as saprophytes.

THE FACTOR OF SAFETY IN THE PULMONARY CIRCULATION.

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The excess of pulmonary air space above the actual needs of the individual, as indicated by the astonishingly large proportion of lung tissue frequently found impermeable to air in pneumonia and tuberculosis, has led to numerous experiments to determine the minimum amount of lung substance compatible with life. Da Fano[1] has recently reviewed the literature. Dogs and rabbits appear to have been used exclusively in these experiments. Da Fano and others have removed one lung and found that their animals lived comfortably. Hellin[2] also studied the exchange of carbon dioxide

[1] Virchows Arch., 1912, ccvii, 160.
[2] Arch. f. exper. Path. u. Pharmak., 1906, iv, 21.

and oxygen in his one-lunged animals and failed to detect any change from the normal. Courmont[3] removed three-fourths and Bernard, Le Play and Mantoux[4] removed five-sixths of the total lung volume and had their animals survive.

In all of this experimental work emphasis has been laid upon the excess of available air space over the actual necessities of the animal. Little attention, apparently, has been paid to the factor of safety in the pulmonary circulation. Pulmonary circulation and pulmonary ventilation are at least of coördinate importance. Meltzer[5] in his Harvey Society Lecture, discusses specifically only the latter.

An approximate estimation of the factor of safety in the lesser circulation may be arrived at in a number of ways. In the first place the amputation experiments referred to above indicate an excess of vascular space as well as of ventilation. Lichtheim[6] ligated branches of the pulmonary artery and determined the effect upon the systemic arterial pressure. He concluded that from two-thirds to three-fourths of the pulmonary vessels may be occluded without affecting the systemic pressure. This has been confirmed by Tigerstedt[7] and by Gerhardt.[8] Finally, the occlusion of the vessels of the lungs may be induced by the injection of neutral oil into the veins. The results of such an experiment may be estimated (*a*) by comparing the weight of the animal with the amount of oil necessary to produce a fall in arterial pressure; (*b*) by roentgen-ray examination of the lungs of animals injected with a suspension of bismuth subnitrate in olive oil; (*c*) by microscopic examination of sections specially stained for fat.

In a series of experiments reported elsewhere[9] it was shown that approximately 1 c.c. of olive oil for each pound of body weight (2.2 c.c. per kilo) must be injected intravenously in order to induce a permanent fall in arterial pressure in dogs. It was shown, further, that when this "critical quantity" was exceeded even by 2 to 5 c.c. the animal usually succumbed very quickly.

A number of dogs were injected with a suspension of bismuth subnitrate in olive oil. In all of these experiments the animals were under ether anesthesia, the systolic pressure was taken from the carotid artery and the oil-bismuth mixture was injected through a cannula in the femoral vein and washed in with a few cubic centimeters of physiological salt solution. Fig. 1 is a roentgen-ray picture of the lung of a 35-pound dog (No. S 11) which, during a period of one hour and ten minutes, received intravenously 37 c.c. of olive oil-bismuth subnitrate mixture in doses of 2 to 3 c.c. At the begin-

[3] Compt. rend. Soc. de Biol., 1912, lxxiii, 503.
[4] Jour. de Physiol. et de Path. gen., 1913, xv, 16.
[5] Harvey Society Lectures, 1906–07, p. 145.
[6] Quoted by Tigerstedt, loc. cit.
[7] Ergeb. d. Physiol., 1903, ii, 554.
[8] Ztschr. f. klin. Med., 1905, iv, 195.
[9] Simonds, J. P.: Jour. Exper. Med., 1918, xxvii, 539.

ning of the experiment the carotid pressure was 165 mm. of mercury. During the hour and ten minutes of oil injections and continuous ether anesthesia the pressure gradually fell to 130 mm. of mercury. The carotid pressure continued to decline slowly and the animal expired one hour later. Postmortem examination showed a moderate dilatation of the right side of the heart, general venous stasis and marked edema of the lungs. The completeness of the injection of the pulmonary vessels is best seen along the margins, where almost every

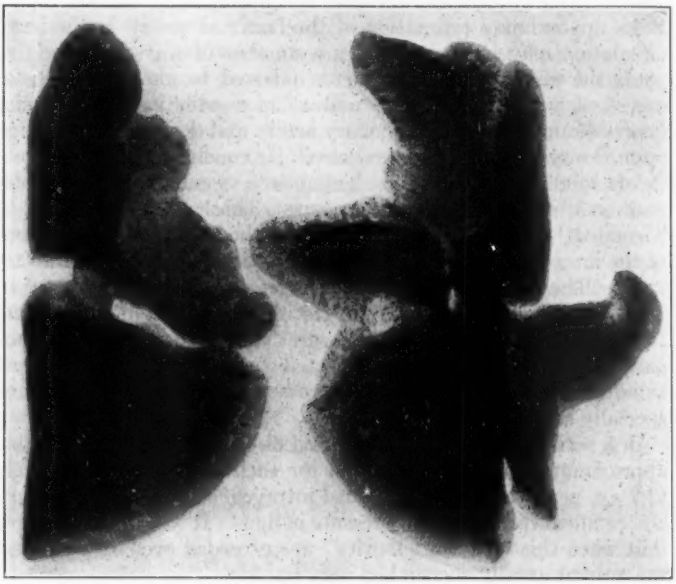

FIG. 1

vessel of sufficient size to obstruct the rays appears to be filled with the bismuth suspension. This animal lived a full hour with its lungs thus injected.

Fig. 2 is a photomicrograph of a section of lung stained with osmic acid from an 18-pound dog (No. S 17), which received 6 c.c. of olive oil intravenously. The arterial pressure remained unchanged.

Fig. 3 is a photomicrograph of a similarly stained section of lung of a 30-pound dog (No. S 15) injected with 42 c.c. of olive oil in doses of 2 to 3 c.c. During the period of injection (one hour and forty minutes) the blood-pressure fell from 120 mm. of mercury to 100 mm. The animal lived fifty minutes longer, during which

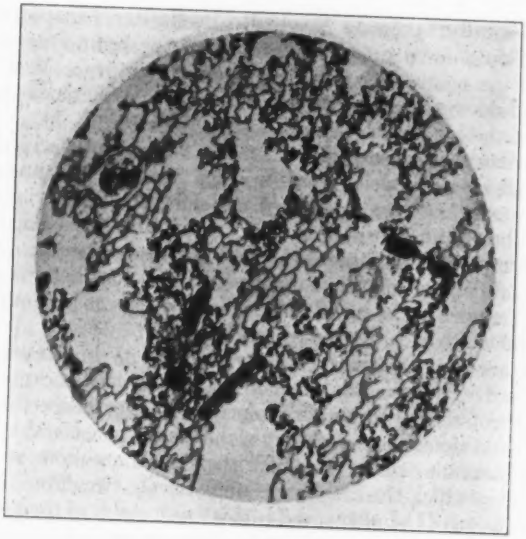

FIG. 2

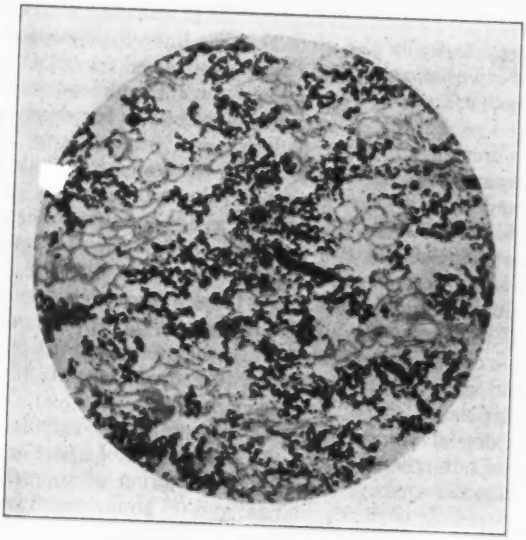

FIG. 3

time the carotid pressure gradually declined. The postmortem examination showed marked dilatation of the right ventricle; the left ventricle contracted and was practically empty; about 40 c.c. of clear fluid was in the pericardial cavity; and there was marked edema of the lungs.

In another series of experiments 0.5 to 0.75 c.c. of sterile olive oil per pound of body weight was injected with aseptic precautions into the saphenous veins of dogs under ether anesthesia. These animals showed no clinical disturbance during the succeeding twenty-four to forty-eight hours except a tendency to dyspnea on exertion. At the end of this time these dogs were again anesthetized and the systolic pressure in the carotid artery taken. It was not found to be below the average for normal dogs.

There are two elements in the factor of safety in the pulmonary circulation. The *primary* element has to do with the pulmonary vessels themselves. In the first place there is evidence that under normal conditions there is present in the lungs a considerable amount of "dead vascular space" in which the vessels are more or less collapsed or in which the blood does not actively circulate. This was the conclusion of Cohnheim and Litten[10] as a result of their attempts to inject the lung through the pulmonary artery. This interpretation appears to have been accepted by Lichtheim[6] and by Tigerstedt.[7] Ghoryeb and Karsner[11] have called attention to the remarkably free anastomosis and early division into capillaries of the pulmonary artery. Finally, and most important, the vessels of the lungs very readily undergo passive dilatation. Their walls are relatively thin and the capillaries in the alveolar walls have little support. The existence of vasomotors in the lungs, as Howell remarks, "has not been demonstrated." The pressure in the pulmonary artery is relatively low, the observed average pressures for dogs collected from the literature by Tigerstedt[7] ranging from 16.9 to 29.6 mm. of mercury. Hence, the dilatation of these vessels is probably purely passive and is dependent upon the volume of blood in the lungs, with or without increase in pressure in the pulmonary artery.

The *secondary* element in the factor of safety in the pulmonary circulation is the readiness with which the right ventricle is able to increase its work and even to hypertrophy when necessary. It may be stated, as a general rule, that any obstruction in the pulmonary circulation of sufficient degree to raise the pressure in the pulmonary artery and of sufficient duration will result in hypertrophy of the right ventricle.

A blocking of any considerable portion of the vascular area of the lungs results, therefore, in (*a*) an opening up of a part or all of the "dead vascular space;" (*b*) passive dilatation of the still patent vessels, especially of the capillaries; and (*c*) an increased pressure in

[10] Virchows Arch., 1875, lxv, 99.
[11] Jour. Exper. Med., 1913, xviii.

the pulmonary artery due to increased energy of the contractions of the right ventricle. As a result of the action of one or all of these elements the amount of blood which reaches the left ventricle is not diminished until the obstruction reaches excessive proportions. It is conceivable, however, that the sudden occlusion of a very large proportion of the vascular area of the lungs, as when a large embolus plugs one of the primary branches of the pulmonary artery, may cause the adaptive mechanism to break down and death rapidly ensue.

The importance of the secondary element in the factor of safety—that is, the ability of the right ventricle to increase its energy of contraction—is shown in the cases of the experiments described above. In Dog No. 17 (Fig. 2) at least one-half of the vessels of the lungs appear to be plugged with droplets of oil, without a fall in arterial blood-pressure. In those animals allowed to live for twenty-four to forty-eight hours after the injection of the oil a still greater proportion of vessels must have been occluded, for the amount of oil per pound of body weight was greater than in the case of Dog No. 17. These animals survived without any reduction of arterial pressure. Dogs No. 11 (Fig. 1) and No. 15 (Fig. 3) had three-fourths or more of the vascular space of their lungs occluded with oil, and yet each survived for an hour after the arterial pressure began to decline. The findings at autopsy indicate that the immediate cause of death in these animals was the failure of the right ventricle, which was always found dilated, and the edema of the lungs. The edema added to the difficulties in two ways: (1) by interfering with ventilation in the already embarrassed lung, and (2) by increasing the viscosity of the blood through loss of fluid. Gauss[12] found that the mere presence of fat droplets in the blood increased its viscosity.

The factor of safety in the pulmonary circulation may have a very practical importance in several ways:

1. It may act as a safety-valve to relieve back pressure in diseases of the left side of the heart. It is thus an essential element in compensation in cardiac diseases. Kuno[13] showed that the blood content of the lungs may vary from 8.8 per cent. to 19.44 per cent. of the total amount of blood in the body. The amount of blood that can be passively stored in the lungs and thus shunted from the general circulation may be as great as 120 per cent. of that normally present in those organs.

2. There is a close relation between the condition of the pulmonary capillaries and the ventilating capacity of the lungs. Peabody[14] has shown that the "pulmonary reserve," that is, the relation between the minute volume of air breathed at rest and the highest minute volume which the patient is capable of breathing, is reduced

[12] Arch. Int. Med., 1916, xviii, 69.
[13] Jour. Physiol., 1917, li, 154.
[14] Am. Jour. Med. Sc., 1917, clv, 100.

in many cases of cardiac disease. "This decreased capacity to breathe deeply may depend upon a change in the elasticity of the lungs which results from an engorgement of the pulmonary vessels. This is in accord with the observation that dyspnea is an earlier manifestation in mitral than in aortic lesions."

3. The factor of safety is responsible for the maintenance of normal systemic blood-pressure in those diseases of the lungs, such as emphysema, chronic interstitial pneumonia, lobar pneumonia and tuberculosis, in which there is an extensive reduction of the total vascular area of the lungs either by destruction or occlusion of large numbers of bloodvessels. It is in this type of cases that the secondary element—namely, increased activity or hypertrophy of the right ventricle, plays an important role; for in practically all of the chronic diseases mentioned above there is some hypertrophy of the right ventricle.

4. It accounts, also, for the difficulty encountered by Mann[15] and others in their attempts to produce fatal experimental pulmonary embolism and for the relative rarity of fatal results in humans following the lodgment of aseptic emboli in the lungs.

It is with pleasure that I acknowledge my obligation to Mr. J. B. Zhingrone, roentgenologist to Mercy Hospital, Chicago, for the accompanying roentgenogram and for numerous others which he kindly prepared in course of these experiments.

[15] Jour. Exper. Med., 1917, xxvi, 387.

REVIEWS

A Diabetic Manual. For the Mutual Use of Doctor and Patient. By Elliott P. Joslin, M.D., Assistant Professor of Medicine, Harvard Medical School; Consulting Physician, Boston City Hospital; Collaborator to the Nutrition Laboratory of the Carnegie Institution of Washington in Boston. Pp. 187. Philadelphia and New York: Lea & Febiger.

Dr. Joslin has given us in this little book a gem of rare value. It is written so that patients of ordinary intelligence can grasp the problems of diabetes and lend intelligent coöperation to the physician attempting to secure for them the maximum safety in health.

Part I gives in untechnical language a rapid survey of the whole subject. Part II retraces with more detail and contains an outline of the treatment of the severer diabetic. Part III contains diet tables and recipes which Dr. Joslin has found valuable in his daily practice; these chapters will prove of great practical value. Part IV gives the simplest tests for the estimation of sugar and acid bodies in the urine, the sugar in the blood and the carbon dioxide in the alveolar air.

Too much can hardly be said in praise of this little volume from the hands of such an eminent authority as Dr. Joslin. C. N. S.

The Orthopedic Treatment of Gunshot Injuries. By Leo Mayer, M.D., Instructor in Orthopedic Surgery, New York Postgraduate Medical School and Hospital, with an introduction by Col. E. G. Brackett, M. C. N. A., Director of Military Orthopedic Surgery. Pp. 250; 184 illustrations. Philadelphia and London: W. B. Saunders Company.

Orthopedic surgery has become of more than ordinary interest since the War on account of the value of this science in the treatment of the mutilating injuries that occur to bones and joints as a result of gunshot wounds. As the author states in his preface, this book is not a treatise on orthopedic surgery, but its purpose is merely to emphasize certain principles and rules of guidance in the treatment of war injuries that have been of value. Treatment is con-

sidered under two main headings: that given at the front and that at the base hospital. Among the many timely subjects presented, the fitting of artificial limbs and the methods of rehabilitation of the wounded are especially well handled. These subjects are most important at this time, and must be of interest to every physician, no matter what line of work he is doing. F. B. B.

OXFORD LOOSE-LEAF SURGERY. By VARIOUS AUTHORS. Edited by F. F. BURGHARD, M.S. (LOND.), F.R.C.S. (ENG.), Colonel, A. M. S., Lecturer on Surgery and Surgeon to King's College Hospital, and ALLEN B. KANAVEL, A.B., M.D., F.A.C.S., Lieut. Col., U. S. A., Associate Professor of Surgery, Northwestern University Medical School. In Five Volumes. Volume I. Pp. 971; 354 illustrations. New York: Oxford University Press.

WITH the appearance of the first volume of the *Oxford Surgery* it may be said that a new era has been reached in the publication of surgical books. The idea of loose-leaf books is certainly not new to the commercial world, where the advantages of such a system have long been appreciated on account of the ease of adding or subtracting sections at will; but this is the first time that any elaborate surgical work has been undertaken along these lines. The great objection that has been raised against the investment in surgical books in the past has been that the return hardly justified the expense on account of the ever-changing views on such matters as surgical technic and treatment, not to mention the constant stream of entirely new problems and important discoveries that come to light. A book that is new today is old tomorrow, and in the past it has been necessary for the surgeon to buy a new book each year, at least, in order to get the latest information, which, as a rule, constitutes but a very small part of any volume, the bulk of most books being practically the same from year to year. Such methods of publication may rightly be considered as wasteful and unnecessarily expensive, and for these reasons this new surgery should appeal to all. The idea of the publishers is to present five volumes, each of which will be kept up to the minute by the publication of quarterly supplements and by merely placing each part of the supplement in its appropriate place, removing obsolete subject matter if advisable, the owner always has the "latest edition." The present volume represents the work of fifteen well-known contributors and deals principally with the surgery of the extremities, antiseptics, anesthetics and transfusion. The effect of the war on surgery is evidenced by the excellent chapters dealing with gunshot wounds and the Carrel method of treating infected wounds.

In spite of the fact that practically every part of the book will probably be subject to revision from time to time, the publishers have not constructed the volume in such a way that it has a cheap appearance, as might have been permissible, but the type and paper are most acceptable, while the binding borders on the artistic. Illustrations are furnished in abundance, and are well chosen, with a view toward elucidation of important subjects. This is especially noticeable in that part of the book dealing with the technic of amputations. F. B. B.

TEXT-BOOK OF CHEMISTRY. By R. A. WITTHAUS and R. J. E. SCOTT. Seventh edition. Pp. 477. New York: William Wood & Co.

THIS book covers both inorganic and organic chemistry, and also includes some discussion of toxicology. The material is so condensed and abridged, particularly the part dealing with general and inorganic chemistry, that it will be of little use to the student who has not had any previous training in the subject. The discussion of the general principles seems to be especially brief and inadequate. The introductory remarks dealing with physical properties will be useful only to the most elementary student.

Such terms as "disodic" (page 41), and "ethylic" (page 51) are obsolescent, and should have been replaced by "sodium" or "disodium" and "ethyl." Other instances of old-fashioned terminology may be found in the book. The use of the expressions "acidulous elements," "amphoteric elements" and "basylous elements" is not strictly correct, inasmuch as the elements in the free state are neither acidic nor basic. The classification in which these expressions are used is a good one, however.

The portion of the book dealing with organic chemistry is much more thorough and modern than the first part. The impression is gained that this part of the book was much more thoroughly revised than the portion dealing with inorganic chemistry. Here the nomenclature is modern and the formulas are correct. An exception to this is found in the case of muscarin, which is given as a trihydroxy compound instead of the usually accepted aldehyde formula. It is doubtful if muscarin ever results from the putrefaction of protein. Lecithin and similar lipoids are much more likely to be its source.

Since all medical students of today have studied both inorganic and organic chemistry in the regular college course, it is difficult to see how a book of the nature of this one can be of any use to them. The book will be of undoubted use to students of pharmacy and dentistry, and others who find it necessary to cover the entire subject of chemistry in a short time. B. M. H.

DISPENSARIES: THEIR MANAGEMENT AND DEVELOPMENT. By MICHAEL M. DAVIS, JR., PH.D., Director of the Boston Dispensary and ANDREW R. WARNER, M.D., Superintendent of Lakeside Hospital, Cleveland. Pp. 438. New York: The Macmillan Co.

Two of the largest dispensaries in this country are managed respectively by the two authors of this treatise. Their observations, therefore, have peculiar value and ought to be of assistance to all who are striving to meet the medical and social needs of the poor. Chapters of their book are devoted to the history of dispensaries; to the fundamental principles underlying the work of dispensaries; to technic, including consideration of building plans; to special types of dispensaries referring briefly to the pay clinic; and to public problems, including the relationship of the dispensaries and the Medical Profession, efficiency tests and financing. Suggestions for by-laws and rules of a dispensary are given at the end of the book.

Too much praise cannot be given the authors for presenting, with such completeness of detail, the many phases of this most important work. Differences of opinion naturally exist, and unfortunately the tendency of most organizers and administrators of hospitals and dispensaries is to forget that the greater charity is from the hands of the physicians giving their time and energy to medical service for the poor. The humanitarian motive or instinct actuates the physician more than the thought of gaining professional proficiency, a position not appreciated often by financial contributors to dispensaries or those who make their living in such work. Had the authors viewed the situation a little more from this viewpoint a truer presentation would have been made. Of particular interest are the chapters on records and statistics; on follow-up systems; on finance and efficiency tests. The book, as a whole, is a very valuable contribution to the rapidly increasing literature on this subject and with the possible exception of the above-mentioned criticism is all that could be desired. C. N. S.

DISEASES OF THE HEART: THEIR DIAGNOSIS, PROGNOSIS AND TREATMENT BY MODERN METHODS. By FREDERICK W. PRICE, M.D., F.R.S. (Edin.). Pp. 472. London: Oxford University Press.

ALL physicians of every specialty are concerned regarding the heart, and therefore to all physicians a complete authentic treatise on diseases of the heart will appeal. The above book is from the hands of one eminently qualified to write authoritatively. Dr. Price was for many years associated with Sir James Mackenzie and Professor Cushny, both of world-wide reputation. The chapters

are all written with the very evident intent of being practical and useful, but with detail sufficient to explain all the interpretations. The analyses are all made in the light of studies by means of the clinical polygraph and the electrocardiograph, but there is included an account of such knowledge of the diagnosis, prognosis and treatment of cardiac disorders as was in our possession prior to the introduction of these more recent methods.

Of special interest at this time are the chapters on chronic valvular disease in view of the enormous number of observations made in our own army camps. Some differences of opinion are naturally noted. For instance, Goodman recently observes that in mental stenosis at Camp Jackson the blood-pressure was usually above normal, while Price refers to it as being usually below normal. The chapter on carditis—the rheumatic infection of the heart in childhood—and the chapter on congenital heart disease are exceptionally well written.

The book ends with an excellent chapter on clinical electrocardiography, which is described as clearly and fully as the reviewer has seen anywhere. C. N. S.

COMPENDIUM OF HISTOPATHOLOGICAL TECHNIC. By EMMA H. ADLER, formerly Technician in the Pathological Laboratory of the Presbyterian Hospital of New York. Pp. 92. New York: Paul B. Hoeber.

THIS little book modestly aspires to supply the student untrained in laboratory work with a brief and handy account of histological technic, and serves this purpose in an admirable manner. The directions are clear and the text and formulas quite free of errors; the work is well adapted for the beginner, but may be improved upon by including interleaves for notes. J. A. K.

A MANUAL OF GYNECOLOGY. By JOHN COOKE HIRST, M.D., Associate in Obstetrics, University of Pennsylvania. Pp. 466; 175 illustrations. Philadelphia and London: W. B. Saunders Company.

IT can hardly be said there is a scarcity of works on gynecology, but very often, in spite of the possession of several books on this subject, the student, as well as the practitioner, finds it difficult to get the information he wants quickly. This presentation of Dr. Hirst's has been prepared for the purpose of giving the medical student a concise and accurate outline of the subject without the need of voluminous reading. The author's many years of experience in undergraduate instruction renders him peculiarly fitted to fulfil this mission, as it is only by close and intimate contact with

students that one can grasp their needs. The book, though small, contains practically all the essential matter that any of the larger books contain, and is thoroughly up to date. It will undoubtedly appeal to students on account of the didactic manner in which most of the subjects are written, but it is doubtful whether it will enjoy much popularity among practitioners, as it presents very little in the way of that personal element which most physicians require of a new book. Special chapters have been devoted to abnormalities of menstruation and leucorrhea, and although criticism may be directed against the discussion and treatment of mere symptoms, from a practical standpoint these chapters will often be of considerable use to the young practitioner in cases in which it is advisable to temporize. The chapter on cystoscopic technic might have been omitted, as it has obviously no place in a book of this kind. Radiotherapy and endocrinology are reviewed briefly but sufficiently to give the student the most recent accepted facts on these subjects. F. B. B.

VACCINES AND SERA IN MILITARY AND CIVILIAN PRACTICE. By A. GEOFFREY SHERA, B.A., M.D., B.C. (Cantab.), Clinical Pathologist to the British Red Cross Hospital, Netley. With an Introduction by Sir CLIFFORD ALLBUTT, K.C.B., M.D., F.R.S., Regius Professor of Physic, University of Cambridge. Pp. 226. London: Henry Frowde and Hodder & Stoughton.

THIS pocket manual aims to record the author's experience with vaccines and sera in military and civilian practice, and evidently, according to the text, his experience has been very satisfactory, especially with vaccines; he has aimed "to furnish an answer of some kind to those who are trying to discredit and discourage specific therapy" and to render his work of material use to general practitioners. The book is written in a simple and semipopular style, is generally good, and probably fulfils, in large measure, the aims of the author. Vaccines have received particular attention in the prophylaxis and treatment of a wide variety of infections, including wounds, and covers about 120 pages; the author is particularly impressed with the efficacy of autogenous vaccines and generally decries the use of stock commercial products. The therapeutic use of the tuberculins is condemned as being neither justified by use nor supported by experimental evidence. Minor errors are occasionally found; one is surprised to read on page 19 that the "toxin" of anaphylaxis is elaborated by the liver, and the term "parasyphilis" (page 191) is now generally regarded as obsolete. Sir Clifford Allbutt has contributed an interesting introduction, and expresses his belief that in vaccination great possibilities lie hidden and that failures occur largely because we are as yet far from understanding the use of the weapon. J. A. K.

TUMORS, INNOCENT AND MALIGNANT: THEIR CLINICAL CHARACTERS AND APPROPRIATE TREATMENT. By SIR JOHN BLAND-SUTTON, LL.D., F.R.C.S., Surgeon to and Chairman of the Cancer Investigation Committee of the Middlesex Hospital, etc. Sixth edition. Pp. 790; 383 illustrations. New York City: Paul B. Hoeber.

THE appearance of a sixth edition of this book indicates that in spite of its rather limited, though none the less important scope, it continues as one of the standard works of its kind. There are evidences of a revision throughout and a few new chapters have been added. The author's views concerning the relation of septic organisms to cancer seem a bit dogmatic, and to state that the degree of malignancy of a tumor varies directly as its exposure to pathogenic organisms needs more proof than has been presented. The use of radium in the treatment of neoplasms is mentioned, but no enthusiasm is exhibited over the results to be attained. In number the illustrations are sufficient; in style they belong to the books of a few decades ago, when wood-cut illustrations were all that could be desired. F. B. B.

PATHOLOGICAL TECHNIC. A PRACTICAL MANUAL FOR WORKERS IN PATHOLOGICAL HISTOLOGY AND BACTERIOLOGY. By F. B. MALLORY, M.D., Associate Professor of Pathology, Harvard Medical School, and J. B. WRIGHT, M.D., Pathologist to the Massachusetts General Hospital. Seventh edition, revised and enlarged. Pp. 555; 181 illustrations. Philadelphia and London: W. B. Saunders Company.

THAT this book has reached the seventh edition is proof of its popularity and that it amply fulfils the designs of the authors as a book for practical use in pathological laboratories, both as a guide to beginners and as a source of reference for the advanced; indeed, but few laboratories are without a copy of Mallory and Wright.

In this edition the authors have added much new matter scattered throughout the book, but the reviewer was surprised to find that no mention has been made of a technic for determining the hydrogen ion concentration of culture media which is supplanting the older methods of titration; likewise, he believes that the authors should include a description of the preparation of normal and decinormal solutions of sodium hydroxide and hydrochloric acid. The section on postmortem technic could be improved upon by including more illustrations, while the chapters on clinical pathology and serological technic should either be made more complete or omitted altogether, yielding more space for descriptions of bacteriological technic.

The pages of the present volume are smaller in size than in the former editions, rendering the book compact and handy; the text is clear and maintains the high order of general excellence and usefulness of this well-known work. J. A. K.

SYMPTOMS AND THEIR INTERPRETATION. By JAMES MACKENZIE, Lecturer on Cardiac Research, London Hospital. Third edition. Pp. 318; 19 illustrations. New York: Paul B. Hoeber, 1919.

THE two appendices, added in this the third edition, deal with topics quite in accord with the point of view and subject-matter of the book itself. In one is a summary of a surgeon's study of hyperalgesic points in several series of abdominal cases which came to operation. This independent study corroborates certain of the author's conclusions regarding the reflex symptoms of visceral disease and exemplifies the value of the line of study of symptoms laid down in this book. In the other the author gives suggestions to those who have asked for guidance in matters of research in clinical medicine. These suggestions are very characteristic of the author's outlook, resulting, as they do, from his own experience. In the first place he evidently considers research in clinical medicine to be the most difficult of all varieties of medical research, because of the large background of experience which it requires. At any rate, he thinks that only those are fitted who have discovered their problem for themselves, and this must come in the ripeness of experience. The field which he believes open to the general practitioner above all others is the study of the early stages of diseases, the prehospital stage, where the subjective symptoms are apparent to the patient, but the signs indefinite or undetectable to the observer. The correlation of these earliest symptoms with the later course of the disease would lead to an increase in our knowledge which would tend to earlier diagnosis and more efficient early treatment. These and other suggestions add a new feature of interest to this original and stimulating book. W. H. F. A.

STUDIES IN THE ANATOMY AND SURGERY OF THE NOSE AND EAR. By ADAM SMITH, M.D., Past Instructor in Operative Surgery, Columbia University Medical College. Pp. 157; 45 illustrations. New York: Paul B. Hoeber.

THE anatomical basis of the present volume is constituted principally by a series of frontal and sagittal sections of the entire head,

which have been selected as showing to advantage structural relationships of importance in treatment, surgical or otherwise. These sections are shown in full-page plates, with descriptive text on the opposite pages, in the manner of an atlas. This part of the book forms Chapter III, a contribution to the anatomy and surgery of the nose and its sinuses. Such sections are always interesting and instructive, and the illustrations portray these for the most part in clear diagrammatic form. Some areas of the sections are left, however, quite undeciphered, perhaps intentionally, but it is a little unfortunate that the artist did not use a more distinctive technic for the various constituent tissues in some localities, as in the portrayal of uvula, inferior turbinate and tongue in Plate XI. Also, in some places, minor distortions incidental to the preparation of the sections have not been rectified before the artist began his work, and these naturally do not aid in a clear understanding of the normal relations. For the main points which the author emphasizes, however, the illustrations are entirely adequate. Other chapters treat of nasal breathing, treatment of intranasal conditions, removal of the pituitary gland, postural treatment of otitis media and mastoiditis and anatomy and surgery of the temporal bone. In these the author elucidates many points in treatment in which he inculcates constantly the lesson on the importance of a thorough knowledge of the anatomical relations. In making clear this method of procedure the author has been most successful, and the book must be regarded as a helpful addition to the literature. W. A.

Neoplastic Diseases. A Text-book on Tumors. By James Ewing, M.D., Sc.D., Professor of Pathology, Cornell University Medical College, New York City. Pp. 1027; 479 illustrations. Philadelphia and London: W. B. Saunders Company, 1919.

The demand for books which are solely devoted to such a special subject as oncology has not been very great in the past, and, as a result, there have been comparatively few works of this kind presented, especially by American investigators. During recent years however, there has been considerable interest shown in neoplastic diseases, more especially the malignant types, and many masterly monographs have appeared from American laboratories and clinics. The time is ripe, therefore, for the appearance of an exhaustive collective review, as it were, which will place before the English-speaking profession all that is known about these most interesting pathological processes, giving due credit to all who have been earnestly working in this special field.

Upon critical analysis we find this book divided into two main sections: one dealing with general and one with special oncology.

The section on general oncology begins with a most interesting and complete as well as highly instructive chapter on the historical phase of the literature on tumors, the references dating as far back as 1500 B.C. The various theories concerning the etiology of neoplasms are presented at length and ably discussed, and a most complete chapter on experimental cancer research forms a very valuable section. Under special oncology the various organs and regions of the body are considered as affected by neoplastic formations. Each chapter in this section may truly be considered a monograph by itself. Naturally the treatment of these conditions is not an important part of this book, but under each disease enough treatment and prognosis are discussed to give the reader a more than ordinary insight into the latest views of the profession. A glance at the lengthy bibliography that is given at the end of the book will suffice to impress the reader with the enormous amount of labor that has been expended in the preparation of the book, and, moreover, it presents in concise form a wonderful index to the world literature for those that care to go even further into the subject than the author has gone. The author is to be congratulated upon the enormous amount of material and statistical data that he has been able to gather into this one volume, and it can reasonably be expected that this work will be freely used and quoted in the future by numerous contributors to scientific literature.

Without any desire on the part of the reviewer to be hypercritical, mention must be made of the absence of a chapter dealing with tumors of the umbilicus. Although such growths are comparatively rare and unimportant, in the light of Cullen's recent monograph a short discussion, at least, should have been included in this otherwise excellent book. The subject-matter is amply illustrated with photographs of the clinical appearance of the various neoplasms as well as with many beautiful photomicrographs. While the work is essentially one on pathology, as stated before, it contains so much practical information on the clinical course of these diseases that it will be of unlimited use to the scientific practitioner. F. B. B.

PRINCIPLES AND PRACTICE OF OBSTETRICS. By JOSEPH B. DELEE, A.M., M.D., Professor of Obstetrics at the Northwestern University Medical School. Third edition. Pp. 1089; 949 illustrations. Philadelphia and London: W. B. Saunders Company.

THIS book needs no introduction to the profession, since it became one of the foremost works on obstetrics as soon as it was published. The author was particularly fortunate in being able to obtain foreign literature throughout the war, and he has used it to good advantage in the present edition. The book is slightly larger than the previous

editions, due to the addition of new material in connection with operative procedures and anesthesia as used in obstetrics. The author has never been a great advocate of "twilight sleep," and his views on this subject have not been changed in the light of more recent experience. Nitrous oxide and oxygen anesthesia have been useful, but the administration must be under the direction of an expert anesthetist. The general high standard of the previous editions has not only been maintained, but additions, revisions and corrections have been made wherever such changes have been necessary. The reviewer would find it difficult to criticise other than favorably such a masterly volume. F. B. B.

EQUILIBRIUM AND VERTIGO. By ISAAC H. JONES, M.A., M.D., Instructor in Neuro-otology, University of Pennsylvania Medical School: With an Analysis of Pathological Cases. By LEWIS FISHER, M.D., Laryngologist and Ontologist, Mt. Sinai Hospital, Philadelphia. Adopted as Standard for Medical Division, Signal Corps, Aviation Section. By Surgeon-General and Chief Signal Officer, U. S. Army. Pp. 444; 130 illustrations. Publisher: J. B. Lippincott Company, 1918.

SINCE the announcement of Bárány's very important studies of the static labyrinth, quite a number of years ago now, we have been waiting with a great deal of impatience for the appearance of an ably written text-book on this subject. We are perfectly conscious of the excellent publications of Friesner and Braun: one on the "Labyrinth" and the other on "Cerebellar Abscess," and would like to take this opportunity of expressing our high opinion of these works. Nevertheless, the subject of "Equilibrium and Vertigo" is for the first time being treated in its entirety in this publication of Jones, which we, therefore, welcome with enthusiasm as a very important addition to medical literature. The author has succeeded in presenting a complex subject in a very simple and at the same time comprehensive manner, and by the very free use of pictures and diagrams, backed by a very clear style of writing, has cleared away unimportant details and put forward the important facts which are necessary in making accurate diagnoses.

The book is divided into two parts: the first part dealing with the practical uses of a study of the internal ear, and the second part being devoted to the real study of the internal ear itself and its ramifying connections. We might perhaps divide off the last chapter into a third part, as it consists of a series of pathological cases very beautifully written up and analyzed by Dr. Lewis Fisher, and is a very important and instructive addition to the book. Some 240 pages are devoted to this chapter.

The first nine chapters, making up the first section of the book, could be read with advantage by every general practitioner, as they put forth very forcibly the importance of the internal ear in its relation to certain general disturbances, which unless this relationship is understood cannot be properly diagnosed and treated. Perhaps the author's enthusiasm will give one who gets his first knowledge of the internal ear mechanism from a reading of these chapters the feeling that the writer believes the summit of neurological diagnosis has been reached. We rejoice in this impression, and though the summit may not be reached, we are much higher up the ladder since the recognition of the importance of the kinetic-static labyrinth. We must, however, criticise the statement of the author that seasickness results from overstimulation of the semicircular canals. Unquestionably, the internal ear is responsible for this disturbance, but it is due to the stimulation of the maculæ of the utricle and saccule rather than of the semicircular canals. The absence of nystagmus and sensations of turning in seasick persons seems to us to prove the above statement. On the whole, however, there is very little adverse criticism that can be properly made. It is a fine text-book. The illustrations are numerous, and, what is important, also instructive. We might wish that the captions were a little more descriptive, especially those dealing with the anatomy. The use of reproductions from moving-picture films is a new idea, and though they seem to take up a lot of room, really convey the phenomena of past-pointing, etc., better than any other method of illustration known to us. The majority of the anatomical illustrations are stereoscopic photographs. G. B. W.

PROGRESS
OF
MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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A Report on Goitre among Draft Men from the Northwest.—BRANDEL and HELM (*Arch. Int. Med.*, January, 1919, No. 1, vol. xxiii) state that during the May and June examinations of Western drafted men at Fort McDowell, California, a remarkable number of thyroid enlargements were noticed. Many were unassociated with toxic symptoms. A considerable proportion, however, had true hyperthyroidism and were unfit for general military service. As a result of their observations the authors conclude that goitre is more common in young men than the experience of the general practitioner would suggest. There are definite goitre districts in Oregon, Montana and probably in Nevada. Locality appears to be much greater in importance than family tendency. Many of the goitres in draft men are unmistakably toxic and should be a cause for rejection. The more toxic cases show a tendency to nephritis in addition to the classical cardiac symptoms. The authors believe that all men having thyroid enlargement should be examined systematically for evidence of cardio-renal pathology.

Non-specific Therapy in Arthritis and Infection.—BRANDEL and HELM (*Arch. Int. Med.*, January, 1919, No. 1, vol. xxiii) report a study of the changes in the blood consequent on the intravenous injection of typhoid protein, when the analogy between the typhoid paroxysm and the malarial paroxysm was considered. The typical reaction following the injection of a foreign protein is characterized

by chilliness or a definite chill, fever, pain, sweating and characteristic changes in the form elements of the blood. A leukopenia followed by leukocytosis was sometimes of very marked degree. The authors studied a series of ten cases. These are reported in detail and graphically illustrated by charts and tables. They conclude that the intravenous injection of typhoid protein (vaccine) almost invariably initiates a leukopenia, followed by a leukocytosis which is associated with but not necessarily proportional to the pyogenic reaction. The induced leukocytosis is chiefly polymorphonuclear, even in those cases in which there is an initial lymphocyte increase. Atypical cell forms, particularly in the lymphocyte group, occurs. Accompanying these there are nucleated reds and myelocytes. The authors believe that during the leukopenic stage polynuclears leave the blood stream and enter the tissues; that the subsequent increase in cells is due to an overproduction of cells from the respective mesenchymal fundaments, as is witnessed by the presence of myelocytes and nucleated cells. The temperature reaction and the clinical findings are not in the nature of an anaphylactic response, as is shown by the absence of eosinophilia. The cyanosis observed is not due to methemaglobin. Improvement is most marked following those reactions in which there is a good myelocytic response. This is probably a measure of the capacity of the body to react. It is believed that dead protein is the common etiological factor, that typhoid protein paroxysm, like the malarial paroxysm, is due not to the presence of new organisms but to the death of the old ones.

Epidemic of Cerebrospinal Meningitis. — CAMAC and BOWMAN (*Arch. Int. Med.*, January, 1919), from observations made at General Hospital No. 6, Fort McPherson, Ga., found that in the winter of 1917 and 1918, cases show no uniformity of symptoms or signs. The most uniform, however, were headache, 100 per cent.; fever, 80 per cent.; delirium, 60 per cent.; vomiting, 60 per cent.; Kernig, 50 per cent.; episthotonos, 30 per cent.; orthotonos, 20 per cent.; but no cases presented the hemorrhagic spinal spotted rash, but possibly the early administration of serum prevented this widespread toxic effect. Although this may be possible, the reviewer has seen epidemics before the serum treatment was commonly used in which spots were only rarely present and in which the symptoms were so varied and misleading that patients were admitted to all the different services of a large general hospital, cases being mistaken for appendicitis, when abdominal symptoms predominated, for uremia, eclampsia, pneumonia and various other conditions. In two of the cases there were no signs except fever and delirium. Early diagnosis is of the greatest importance and in many cases this is only possible by lumbar puncture and examination of the spinal fluid. It is particularly important that this should be done in cases of fever and delirium with no other physical signs, and that one should have everything ready to administer the serum. If the spinal fluid is cloudy or is clear, with physical signs of meningeal involvement, give 20 to 30 c.c. of antimeningococcus serum. Two such treatments should be given every twenty-four hours for the first few days and decrease as the patient improves physically. If the patient shows marked toxic symptoms or is doing

badly, intravenous treatment should be tried; 50 to 60 c.c. as often as once every twenty-four hours. This may be followed by rise in temperature to 103° or even 105°, and commonly by chill, but this is often followed by drop to normal or even subnormal, and should cause no alarm. Herrick has reported successful use of intravenous meningococcus serum at Camp Jackson in certain instances. Intravenous treatment should bring favorable results when intraspinal method seems to fail. The temperature is of practically no value as a guide as to when serum therapy should be discontinued. The most reliable guides are the spinal fluid and the general condition of the patient. The spinal fluid should be clear and free from meningococci. The patient should be clearly in much better condition and free from delirium and toxic signs.

SURGERY

UNDER THE CHARGE OF

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Repair of Large Gaps in Peripheral Nerves by Neuroplasty.—MACKENZIE (*Surg., Gynec. and Obst.*, 1918, xxvii, 353) says the object of his study was three cases which illustrate the utilization of nerve flaps of both central and peripheral origin in order to bridge unusually large gaps in peripheral nerves. He concludes that regeneration and recovery of function are promoted by the use of nerve flaps and that both central and peripheral flaps can be used for such purposes. A peripheral flap by laying down a nerve path may promote regeneration over a great gap; in one case quoted regeneration occurred over a gap of ten and three-quarter inches. The approximation of nerves and their repair should be done in all cases with the least possible delay. (This would apply as well to cases which are infected as to clean cases.) The arrest of trophic shock can be promoted by early closure of large gaps by flaps. Unimpaired nerve tissue should always be utilized for the effective repair of damaged nerves. In their repair, nerves can be successfully sequestrated in muscular tissue, so as to promote their own regeneration and that of the muscles in which they are embedded. The principle of sequestration (burial in or covering over by muscular tissue) can be utilized in proper cases so as to avoid infected zones in wounds and also scars and other obstacles to nerve repair. The theory has been held for a number of years past that regeneration can only take place from the central end of a nerve, and more recent studies would tend to confirm this principle. That regeneration on a colossal scale can take place, and has taken place, under conditions in which flaps taken from the peripheral ends of a

divided nerve and utilized to bridge a gap ten and three-quarter inches in length and fixed to the central end of the divided nerve, and that they were successful in restoring motion and power to muscles completely paralyzed by the trauma, is manifest in view of the results obtained in the case referred to above and listed as follows: (1) Trophic recovery is practically complete. (2) There has been recovery in a limited degree of protopathic and epicritic sensibility. (3) There is almost universal recovery of deep sensation. (4) Recovery has taken place of motion and power in groups of muscles which, after the excision of the nerve, were reduced to a hopeless state: (*a*) The flexor group in the thigh, viz., complete recovery of the semimembranosus, semitendinosus and the biceps; (*b*) the flexor group in the leg, viz., the gastrocnemius, plantaris, soleus and popliteus. Extensive recovery has taken place in this group which has been progressive; (*c*) the extensors and flexors in the phalanges and foot. (5) The relatively small and contracted area of absolute cutaneous analgesia. (6) The relatively small area of thermic analgesia. (7) The direct sensibility of the nerve to deep pressure and the transmission of painful sensibility thereby to the foot. (8) Possession of muscular sense. (9) Independent and unaided locomotion; the man can not only walk long distances but can run at considerable rate of speed.

Lesions of the Sacro-iliac Joint. — COFIELD (*Am. Jour. Orthop. Surg.*, 1918, xvi, 418) says that a careful study of the anatomy and functions of the sacro-iliac joints precludes the possibility of subluxation or relaxation occurring except in severe crushing injuries or possibly during the later stages of pregnancy, when all pelvic ligaments are in a state of temporary relaxation. The symptoms occurring in acute and chronic sacro-iliac lesions, as well as many of the sciaticas, are to be explained by sprains of the joint, the spasmodic action of the posterior musculature of the body and the sequelæ resulting therefrom. Manipulation for the cure of sacro-iliac lesions has in the past been practised by the average physician in a purely empirical way, realizing that it was of service in a certain number of cases. On account of the frequent occurrence of anomalies of the spine and pelvis in this region, a roentgen-ray examination can only be of positive value when checked up by a subsequent examination after a cure has been effected. Traumatic lesions of the lumbosacral articulation may simulate very closely those of the sacro-iliac joint and may require a similar method of treatment.

Roentgenological Aspects of Hour-glass Stomach.—CARMAN (*Surg., Gynec. and Obst.*, 1918, xxvii, 426) says that hour-glass stomach should not be considered a disease entity but an end-result of various pathological processes, gastric and perigastric. The possibility of congenital hour-glass stomach must be admitted, although most cases reported must be questioned. The roentgenogram usually shows a much deeper constriction than is seen at operation, due to the fact that the organic narrowing is exaggerated by the spasm. Cases of spasmodic hour-glass, whether intrinsic or extrinsic in cause, are not seen by the surgeon, because they are relaxed by the narcosis. Therefore, if the hour-glass is the only roentgen sign present, the first thing to do is to

exclude extrinsic causes. Belladonna or atropin does not differentiate between the organic and intrinsic types of spasmodic hour-glass stomach. Belladonna to physiological effect will differentiate between the intrinsic and extrinsic types of spasmodic hour-glass stomach. Operations have proved the organic type the most common. However, the spasmodic, when intrinsic in origin, is just as important from the diagnostic standpoint as the organic. The varieties of hour-glass stomach, therefore, admit of the following subdivisions: Congenital and Acquired: (1) Organic: constriction due to structural changes in or about the stomach. Causes: ulcer, scar of healed ulcer, perigastric adhesions, cancer, syphilis, corrosive, resection, gastrotomy, congenital? (2) Spasmodic (or functional): Cramp of the gastric muscle without structural change. Two types: (*a*) intrinsic; cramp directly produced by lesions in the stomach; causes practically the same as those of organic hour-glass; (*b*) extrinsic; cramp indirectly produced by causes outside of the stomach: duodenal ulcer, diseases of the gall-bladder, disease of the appendix, neuroses, tabes, lead intoxication, morphin, nicotin; (*c*) pseudo- hour-glass; simulating the hour-glass form without either spasm or structural change in the stomach; causes: contraction of the abdominal muscles, pressure of stomach against the spine, tumors outside of the stomach, atonic stomach, gas and fecal matter in the bowel.

Temporary Internal Fixation of Compound Fractures.—Brown and Brown (*Surg., Gynec. and Obst.*, 1919, xxvii, 440) says that, as a result of our war experience, there is more and more stress being laid upon the mechanical cleansing and immobilization than any other two features in the treatment of fractures. Their experience for the past two years has added what they believe to be as important, or possibly more important, and that is the temporary fixation of the fracture, preferably with the Parham-Martin band, or if not feasible, with a Lane plate; this fixation to be removed under local anesthesia at the end of five or six weeks. The internal fixation frequently reduces or solves the problem of extension. They believe that temporary internal fixation of compound fractures should be more frequently used and that it will prevent many of the difficult reparative operations which we have to do on non-union compound fractures. The incidence of infection is not increased but reduced in direct proportion to the fixation. The bands or plates should never be used with the understanding or hope that they will remain permanently. They prevent excessive deformity and relieve pain between and during the dressings. The Parham band is much to be preferred to the Lane plate, where it can be used, because in oblique and comminuted fractures it is a better mechanical support and brings all the fragments into perfect apposition and does not open the medullary cavity with the possibility of infection and osteoporosis. As complete external immobilization should be maintained as would be if internal fixation were not used.

Empyema.—Rockey (*Military Surgeon*, 1918, xliii, 384) studied this subject in connection with his experience at Camp Lewis. Forty-eight cases were operated on; 2 were diagnosed antemortem but not

operated on; 8 were diagnosed only at postmortem; 10 cases of pneumococcus empyema were operated on by rib resection and all 10 were operated on for empyema following measles and 6 recovered; 20 cases of hemolytic streptococcus empyema had only rib resection treatment and 5 died, while 17 more of the same kind had thoracotomy with constant negative pressure treatment and none of them died. The latter is therefore considered the most efficient treatment for the streptococcus empyema. This is shown by: (*a*) absence of mortality; (*b*) smooth postoperative convalescence, except in cases of too early removal of drainage tubes; (*c*) absence of pneumothorax, as proved by the roentgen ray; (*d*) economy of material and labor.

Empyema at Camp Custer. — The Empyema Board of the Base Hospital (*Review of War Surgery and Medicine*, 1918, No. 9, i, 1) summarizes a very illuminating report as follows: In the majority of cases of empyema, a streptococcus has been the causative organism. When grown on blood agar it has been shown to be hemolytic in a large percentage. During the prevalence of empyema, streptococci were demonstrable in a majority of throats of healthy soldiers (including fresh recruits) as well as of patients entering the hospital with respiratory infections. The clinical manifestations include rapid and profound toxemia, the quick formation in many cases of large amounts of pleural exudate and a marked tendency to pocket formation by old and new adhesions in atypical locations. The mortality was highest (61.5 per cent.) in the cases of empyema following measles, lowest (22.7 per cent.) in the cases in which empyema was the primary condition. (Cases following measles not designated primary.) In empyema complicating pneumonia, the mortality was 38.2 per cent.; the mortality of all cases of empyema was 4.5 per cent. At autopsy the outstanding features have been the finding of widespread lesions, with a tendency to involve serous membranes, the occurrence of a severe bronchitis in a majority of cases and a type of bronchopneumonia so distributed as often to resemble a lobar process. Early recognition is important, especially in the acute fulminating types of cases. The diagnosis depends upon close attention to clinical progress, frequent observations accurately made and recorded, and proper interpretation of physical signs. Dulness, the sense of resistance on percussion and the diminution or absence of tactile fremitus are the most reliable signs. The relative incidence of empyema complicating pneumonia was high, one month 50 per cent. of pneumonia cases developing pneumonia. Of 830 cases of measles (including German measles), 4.4 per cent. developed a chest complication of pneumonia or empyema; of this group, empyema was the primary condition clinically in 70 per cent. of cases. The treatment instituted should depend upon the conditions existing in each individual case. No one type of operative procedure should be employed as a routine procedure. Thorough drainage without pneumothorax if possible and with minimum operative procedure seems to be indicated in the acute stage of the fulminating cases. In the cases treated by more radical operation the best results have been obtained by the use of the Carrell-Dakin technic early instituted.

THERAPEUTICS

UNDER THE CHARGE OF

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The Treatment of Severe and Progressive Hemorrhage by Intravenous Injections.—PENFIELD (*Am. Jour. Physiol.*, 1919, xlviii, 121). The blood-pressure of experimental animals was kept at a shock level for various lengths of time by progressive bleeding so that their condition resembled that which must frequently exist in wounded men at the front who have sustained severe and continued loss of blood. After analyzing the condition of these experimental animals according to the duration of low blood-pressure, the amount of blood lost and the degree of acidosis resulting, the author was not able to show that gum-sodium bicarbonate solution or gum-glucose solution is more efficacious in saving life than is an isotonic solution of sodium chloride. By perfusing an isolated vascular bed the author showed that following a large hemorrhage there is a primary constriction of the peripheral vessels. With continued low blood-pressure this constriction passes off and dilatation supervenes. Associated with this dilatation the venous pressure rises while the arterial pressure is falling. All dogs in which the venous pressure rose while the arterial pressure was falling, for a period of twenty minutes or more, died regardless of treatment. The effects of stimulation of the saphenous nerve while these animals were in a condition of profound shock indicated that the reflexes affecting respiration and blood-pressure were not paralyzed, although the author considers that this point deserves more careful investigation.

The Output of Epinephrin in Shock.—STEWART AND ROGOFF (*Am. Jour. Physiol.*, 1919, xlviii, 22) found that the rate of output of epinephrin in dogs and cats, after the blood-pressure had been permanently lowered by exposure and manipulation of the intestines, by partial occlusion of the inferior vena cava, by hemorrhage and by "peptone" injection, was the same as before the lowering of the blood-pressure, within the limits of error of the methods used for assaying the epinephrin. A marked increase in the rate of output of epinephrin was produced by strychnin. (The above is in direct contradiction to the results of the observations reported by Cannon.—Abst.)

A New Treatment for the Morphin Habit.—BLUEMEL'S method (*Jour. Am. Med. Assn.*, 1919, lxxii, 552) of treating the morphin habit is as follows: The patient is put to bed and his morphin stopped entirely. He is put on semisolid or liquid diet and is given cathartics as prescribed in the Towns-Lambert treatment. He thus receives three or four cathartic courses, consisting of 5 grains of blue mass with 5 compound cathartic pills at intervals of eighteen hours. Some hours after the last of these cathartic courses he is given castor oil.

In addition the patient receives from two to four intravenous infusions a day of 1000 c.c. of 0.9 per cent. sodium chloride solution. During the first few days the patient is given enough chloral at bedtime to ensure a night's sleep. Hypnotics are an important part of the treatment, as the sleep so induced blots out large periods of discomfort and fortifies the patient mentally and physically. The liquid diet is continued as long as the patient feels any nausea, and he is kept in bed during the cathartic period and until all acute discomfort from the withdrawal of morphin has disappeared. There seems to be no contra-indication to the saline treatment, and patients showed no ill effects from three or four infusions daily for a period of a week or more. The effect on arterial tension is slight and transient. Repeated infusions do not produce anemia, and the patient shows marked improvement in color. There is a decided decrease in the viscosity of the blood, which lessens capillary resistance and reduces the heart load. It was not found necessary to give cardiac stimulants to any of the patients. Six patients were treated by the foregoing method. Their average age was thirty-four years; the average period of addiction twelve years; the average daily dose of morphin was from 7 to 8 grains. The average amount of saline administered was 15,600 c.c. The stay in the sanitarium averaged fourteen days, during the first seven of which the saline was administered. Discomfort with withdrawal symptoms was not very marked, and was experienced during the first two or three days only. Most of the patients experienced considerable relief from the intravenous infusions. The stage of acute discomfort was followed by a period of nervousness and sleeplessness, which was not constant. The patient usually required hypnotics for only four nights. In two patients, who had been addicts for more than twenty years, the nervousness persisted at the end of the second week, at which time the Towns-Lambert treatment (without morphin) was given as an experiment. The nervousness diminished considerably following this second treatment. The author considers this improvement to point to some specific potency in the Towns-Lambert belladonna mixture, though the effect of the second course of cathartics and the influence of suggestion must be considered. Six other, rather milder, cases were given the Towns-Lambert treatment simultaneously with the infusions. The average age of this series was forty years; the average period of addiction was nine years; the average daily dose of morphin was $3\frac{1}{2}$ grains. Two patients received infusions only when they manifested discomfort under the Towns-Lambert treatment; the other four received infusions from the start. The average patient was given five infusions and the infusions were not continued beyond the third or fourth day. The average patient was discharged on the seventh day. With the combination of the Towns-Lambert and the infusion treatments the patients suffered about the same discomfort as those treated by infusion alone, but they recovered more quickly from the subsequent period of nervousness. Some of them manifested a definite euphoria on the third or fourth day. Thus it would seem that the infusion treatment combined with the Towns-Lambert is better than the infusion treatment alone; however, as the two series of cases were not equivalent, the author feels that further investigation is necessary to determine the matter definitely.

OBSTETRICS

UNDER THE CHARGE OF

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Placental Tissue as a Galactagogue.—CORNELL (*Surg., Gynec. and Obst.*, November, 1918) has experimented with the placenta of cows prepared by washing and drying and then put up in 5-grain capsules. This dose is given four times a day for twelve doses. The first is administered as soon as the patient has recovered from labor and is able to take nourishment; it is usually given within twelve hours after delivery. A few patients objected to the odor, but aside from that there were no bad or disagreeable effects noted. The results were recorded and studied in the last 100 cases in which the preparation was given. As a comparison 70 patients entered the hospital at the same time and were placed on the same floor and were studied under the same conditions. The same food was administered to both groups of patients. The result showed that placental tissue has a favorable effect in the production of milk. Nationality and age of the patient and the sex of the child have nothing to do with the results. Among those mothers who did not receive placental tissue, 69 per cent. of the children began to gain on the fourth or fifth days, while among those mothers who received placental tissue 87 per cent. began to gain on the fourth or fifth day. Forty-four per cent. of the children regained their birth weight before leaving the hospital in cases in which the mother received placental tissue. When the mother was given no placental tissue 24 per cent. of the children had regained their birth weight before leaving the hospital. These results indicate that placental tissue has a definite value in stimulating the production of milk.

Thirty Cesarean Sections.—MCILWRAITH (*Surg., Gynec. and Obst.*, November, 1918) published a paper some ten years ago in which he described a series of twenty-seven labors occurring in women having contracted pelves without Cesarean section. His method of treatment consisted in prophylactic version and in induction of labor. After losing three babies in close succession his method of treatment was changed. In primipara having moderately contracted pelvis the patient was given the test of labor and when this failed a section was done. Among his cases were six whom he described as obstructed labor. In these external measurements gave little or no evidence of internal contraction, but the head failed to engage before or during the first stage of labor. All the mothers made a good recovery and all the children but one, which was malformed. One of the women was thirty-six hours in labor, yet both she and her child made good recoveries. Eighteen months later she was successfully delivered of a second child by section, having declined to risk the loss of the baby by premature labor or to suffer the first stage of attempted delivery.

Another class of his cases were those in whom the pelvis was known to be contracted. Here but one child was lost, which had hydrocephalis. The mother of this child was in the medical ward of the hospital for treatment of a tubercular knee-joint. In placenta previa three cases were operated upon for this complication, mothers and children making good recoveries. The writer believes that this is the best method of treatment for those cases in which the child is viable and there is but little dilatation. In one case of accidental hemorrhage the woman was sent to the hospital after a severe bleeding. The patient was eight and a half months pregnant, bleeding very little after she entered the hospital; the fetal heart-beat was good at 120. Fifteen minutes after the examination the pulse became slow and irregular, and signs of internal hemorrhage appeared. The cervix was tightly contracted and would not admit the finger-tip. On opening the uterus a large black clot, equivalent to about a pint of blood, was found, followed by a few ounces of fluid blood. The placenta had been almost entirely separated. The mother made a good recovery, the child, which weighed $2\frac{1}{2}$ pounds, lived a week. In the toxemia of pregnancy with convulsions the writer believes that when the cervix is not dilated and soft and treatment has failed to prevent or control the convulsion that section is the safest treatment. In cases of toxemia in which threatening signs develop before convulsions occur, prompt operation may save life, and when an anesthetic cannot be given, local anesthesia and gas and oxygen may be employed. Vaginal section is performed in a few cases: one a toxemic woman who had severe convulsions and did not long survive the operation. Another case which showed tuberculosis of the kidneys was treated by vaginal section. The third patient made a good recovery. The writer believes that this operation is well suited for cases of pernicious vomiting. In one case there was a severe chill and temperature of 106° on the fourth day. A small piece of membrane was removed and an intra-uterine douche given, after which the patient's recovery proceeded normally. Three patients were delivered a second time by section, and on examination the uterine scar was sound. As regards the history of the patients who became pregnant subsequent to Cesarean section, the writer believes that if the uterine muscle is properly sutured an infection does not occur there is but little danger of rupture. He sutures the uterine muscle with No. 2 chromic gut and over this places a continuous suture of No. 1 gut. He has as yet seen no bad results.

The Operative Treatment of Chorio-epithelioma.—VINEBERG (*Surg., Gynec. and Obst.*, February, 1919), from his study of the literature of the subject and his own cases, believes there are on record between 500 and 600 cases of this condition. The writer collected in the literature 69 cases and adds 9 of his own, making a series which he studied of 78. Of these 4 were younger than twenty; 13 between twenty and twenty-five; 21 over forty, of whom 8 were fifty or over. The number of cases below twenty and over fifty years is of interest and has some relation to hydatid mole, which is most often met at the extremes of reproductive life. The condition is also found most often in those women who have rapidly conceived. The period of latency varies

from a few weeks to twenty-one years; there can be no doubt but that several years at least can elapse between the last possible gestation and the development of the condition. He quotes Ries's case as illustrating the fact that chorionic villi may remain quiescent in the body for a long time; in his patient on removing a fibroid uterus a vein containing degenerated chorionic villi was hanging from the left uterine cornu. No chorionic epithelia were found on these villi. There had been no possibility of conception for eighteen years, during which the chorionic villi had remained latent. In some cases the condition had already existed before the termination of the pregnancy. Numerous cases are quoted to prove the possibility of this occurrence. The common opinion that this growth followed hydatid mole is borne out by many reports, the percentage being estimated from 48 to 5 per cent. The most characteristic symptom of this growth is hemorrhage from the uterus, which is very profuse and may be alarming. In some cases this requires a prompt application of intra-uterine packing; in others the bleeding is moderate in amount but protracted, and resembles that caused by the retention of a piece of placenta or decidua. When bleeding returns after a curetting this circumstance should excite suspicion. When bleeding is profuse and frequent the patient becomes very anemic, and very often septic infection is added to the complication. In one of the writer's cases, the only fatal one, this occurred. The growth of the tumor usually perforates the uterus and may cause intraperitoneal hemorrhage, which resembles very closely ruptured tubal gestation. Pain is caused by the expulsion of blood-clots, and in some cases is a very annoying symptom. In the latter stages the pain is dull and the broad ligament becomes involved. Hemoptysis is an important symptom; it usually indicates that the disease is attacking one or both of the lungs. Tumors in the vaginal wall, anteriorly near the urethra, varying from an almond to a hen's egg in size, are often among the first symptoms. These tumors are deep bluish in color and appear very vascular. The uterus is usually enlarged to six or twelve weeks and the cervix is in most cases open, admitting the finger, thus giving access for exploration. Hard nodules of varying size will be felt in the uterus, with distinct excavations or hollow in the center. If it can be distinctly proved that this condition has not been produced by curetting, a diagnosis of chorio-epithelioma can be made. In one of the writer's cases a negative report was given by the pathologist for the examination of material removed, but on exploring the uterus with the finger the writer found the characteristic condition and made a correct diagnosis. On the other hand, the uterus may be little or not at all enlarged, and in one of the writer's cases the growth was the size of a cherry, and beneath the peritoneal covering near the left cornu. In some recorded cases there were no manifestations in the genital tract, but the disease showed itself in a tumor of the brain, spinal cord or lung; thus in one case reported the patient was thought to have pulmonary tuberculosis, and chorio-epithelioma in the lung was the condition present. In another the patient developed paraplegia eight months after delivery, and at autopsy the characteristic growth was found in the spinal cord at the level of the fourth lumbar vertebra. The literature shows thirteen cases of chorio-epithelioma in the Fallopian tube, in which

the tumor varied in size from a hen's egg to an adult human head, and was very friable and bled profusely. Metastases are very frequent and take place from the blood stream; most frequent are those in the lungs at the apices or bases, then comes the vagina; the vulva is a most frequent site of metastatic growth. Occasionally a single ovarian tumor is found, but more often small nodules forming an irregular ring. They vary in consistency, size and color, but grow very rapidly, causing necrosis and lacerations. They produce profuse and obstinate bleeding, and soon become infected. The broad ligament, tubes and ovaries may also be attacked, and secondary growths are frequently found at autopsy in the liver; these vary in size and are occasionally as large as a fetal head. A tumor in the kidney may give rise to no symptoms at all, although in some cases the urine contains the characteristic cells. In the central nervous system growths are usually found at the level of the left hemisphere in the occipital lobe. There seems to be no portion of the body in which metastases may not develop. Diagnosis is often very difficult; the condition should be suspected when profuse hemorrhage follows a hydatid mole which has been thoroughly removed. Some years ago the writer urged that in these cases the uterus should be opened so that the hand may be employed to remove all vesicles; in this manner the uterus may be thoroughly examined and malignant growths detected in its very beginning. Repeated curettings are dangerous and should be avoided. In some cases amenorrhea intervenes between the removal or discharge of a hydatid mole and the first symptom of chorio-epithelioma. When growths develop soon after labor has terminated the cervix is usually open and it may be possible to palpate the interior of the uterus with the fingers. If indurated and with hard nodules, with excavations in the center, the diagnosis will be almost certain. When the growth follows an early abortion one may perform curetting and have the scraping examined by a pathologist, but the result of the examination is often misleading; only tissue obtained by very deep curetting will give a positive result on examination, and if this be done the uterus may be injured and particles of the growth may be set free to enter the circulation. The literature shows that the most rapidly fatal cases were those that had several curettings and then hysterectomy. It has been abundantly proved that curetting before operation has greatly increased the mortality. In the writer's series of nine cases there were eight recoveries, an early diagnosis having been made; while in the one patient who died two curettings had been performed. In cases in which the operator desires to avoid curetting he may follow the practice of the writer and perform vaginal hysterotomy, antiverting the uterus through the anterior vaginal incision; in this way the uterus can be palpated and inspected by direct vision. As regard prognosis, if the diagnosis be made early and curettings are avoided, recovery may follow even though there have been extensive metastasis. Growths in the vagina and other portions of the body sometimes disappear spontaneously. Sometimes after the removal of the uterus small growths in the vagina disappear without further interference. Operation as early as possible gives best results, and if the patient is without any sign of recurrence six months after operation the prognosis is good, and after one year it is very much better; after two

years without recurrence, recovery may be considered absolute. The great majority of cases operated upon early recover from the operation and are free from return permanently or for a considerable time. Better results are obtained in cases following hydatid mole, because these patients are watched more closely and diagnosis made early. A considerable number of these cases follow hydatid mole, and the older the patient the more the danger of malignant growth. The writer urges that vaginal hysterotomy be done in these cases to avoid the unnecessary removal of the uterus; as soon as the diagnosis is made the entire uterus should be removed. The abdominal route is usually the best one for this operation; there is less disturbance of the tissue and the deep pelvic veins can often be excised, which is a source of additional safety. There is no necessity for doing an operation so radical as the Wertheim operation, even though the condition seems unpromising. The presence of metastasis in other organs does not forbid operation. Radium has been tried in these cases, but with only temporary benefit. The reports of nine cases are added in detail. The reviewer in a case quoted by the writer had a patient suffering from pernicious nausea, who after the interruption of pregnancy developed symptoms of malignant growth in the brain, death ensuing, and at autopsy metastases were found in the brain, lungs, kidneys and other organs. The first unusual condition present was the pernicious nausea.

The Effect of Hysterectomy upon the Ovarian Function.—RICHARDS (*Surg., Gynec. and Obst.*, February, 1919) has studied the question of the effect of hysterectomy on the ovarian function. He believes that the uterus is not essential for the continuance of ovarian function except as regards menstruation and reproduction. Those who maintain that the ovaries should be removed when the uterus is removed have not furnished convincing evidence of the correctness of their position. Ovarian function is disturbed by hysterectomy because normal menstruation is rendered impossible and during the operation injury is done to the ovary or to its circulation. The bulk of authentic evidence favors the retention of sound ovaries whenever possible.

The Etiology of Toxemia of Pregnancy.—TALBOT (*Surg., Gynec. and Obst.*, February, 1919) believes that fundamental causes of toxemia of pregnancy with or without convulsions are not in the products of conception. He states the case of a woman who after incomplete abortion was curetted and developed mitral stenosis; she soon after became pregnant and had no symptoms of toxemia, but her pulse became very rapid; she was kept in bed and finally delivered by section. Four days afterward she had severe headache; seven days after the operation she had twelve convulsions and died on the following day. The pulse tension had become 180, although the bowels had moved several times daily since the operation. He also reports the case of a pregnant patient with normal blood-pressure and contracted pelvis. The urine was negative, but the patient was suffering from pain in the joints. A month later the face was slightly puffy and numbness of the greater part of the right hand appeared. There were no headache or eye symptoms. The urine was negative as regards albumin, and

but one granular cast was seen. The patient was immediately put to bed and vigorously treated with restricted diet. Albumin increased with casts and labor was brought on and a small male child born, dying twelve hours after birth. The patient recovered somewhat slowly. Six months after delivery it was found that the patient had two bad teeth near the antrum, and when these were extracted, pus was discharged. The writer in a series of 97 cases has found sepsis in the mouth arising from bad teeth in every case without exception; most of these patients had pus pockets at the root of the teeth. The writer describes a case with no evident symptoms of pus about the teeth, but roentgen-rays showed two pockets hidden in the jaw. The writer believes that the focus of chronic sepsis in some part of the body is the cause of the toxemia of pregnancy and not the fact of pregnancy. He believes that the removal of the product of conception often aids the organism to free itself from this toxemia.

Placenta Previa and Cesarean Section.—BOCHEL (*Arch. d'Obst. de Gynec.*, 1918, Nos. 7 to 9) contributes a paper upon this subject, in which he describes the case of a patient, a primipara, about six months pregnant, whose pregnancy had proceeded practically normally. She had, however, been taken with fever and albuminuria, which persisted. She had an abundant hemorrhage, which was treated by tamponing the vagina. When seen in consultation the patient was pale, suffering from blood loss, the cervix long, undilated and firm. The patient was taken to the clinic, where the tampon was removed, and she became slightly better. Attacks of syncopy, however, showed that pregnancy must be rapidly terminated; accordingly Cesarean section was practised and a child, about six months developed, was quickly extracted. The placenta had become partly separated but its substance was healthy, and so were the tissues of the uterus. The patient made a good recovery. She again reported when pregnant, having passed through practically a normal pregnancy, and came to the hospital in labor. She was delivered spontaneously of a living female child of normal weight. There were no complications in the third stage of labor, and the mother nursed the child successfully. In the third pregnancy the patient had a transverse position of the child, with shoulder presentation, for which version and extraction were done without injury to mother or child. Both made good recoveries. This case is cited to show that Cesarean section performed for placenta previa does not necessarily mean that the patient may have difficulty in subsequent labor. The writer discusses at some length the propriety of section for placenta previa, and concludes that in many cases major surgery is unnecessary, but that when such should be indicated, abdominal Cesarean section is the operation of choice.

The Transfusion of Blood for the Hemorrhages in Parturient Women.—GUILLUM (*Arch. Mens. d'Obst. de Gynec.*, Nos. 7 to 9) contributes an extensive review of this subject. He draws attention to Dulbet's statement that women do not die because of the lack of blood cells but because of the lack of serum. On this theory is based the use of saline solution for acute anemia following hemorrhage. In order for the transfusion of blood to be successful, the blood transfused must

cause coagulation in the serum of the person who is to receive it as an evidence of the regeneration of the blood of the anemic person. One questions whether an intravenous injection of serum would not be better than a transfusion of blood. By some it is held that when the red cells have been reduced to 25 per cent. of their usual number transfusion is indicated. In choosing the method for obstetrical cases it must be simple and practical, and one which can be easily applied inside and outside of a hospital. Briau has proposed an ingenious method of the direct joining of artery to vein, which has proved successful. In hospitals cannulæ are employed with good success. Blechman has practised the direct transfusion from vein to vein. Coley, Edwards and Vaughan employ a syringe for venous transfusion. Kimpton has a glass tube by which he performs immediate transfusion. David and Curtis use a glass cylinder with cannulæ. Jeambrau uses a glass bottle whose base is drawn to a point connected by tubes, and in its circuit is a bulb cannule used for the Paquelin cautery. Foley has devised perhaps the most recent practical method for this operation; he employs a glass tube and glass bottle. It has lately been shown that two elements play an important part in restoring patients who have lost blood, one the volume of liquid, the other the number of blood cells introduced. It seems most important to dilute the blood in the serum which is used for direct transfusion. With the aid of paraffin and citrate of sodium, blood may be coagulated in the ampule of Jeambrau or Foley's tube, giving a physiological serum of 8 to 1000, which will be acceptable for transfusion.

The Recognition and Management of Labor Injury.—Skeel (*Am. Jour. Obst.*, January, 1919) contributes a paper upon this in which he urges thorough examination of all parturient patients to discover injuries sustained at labor. After delivery of the placenta, gas analgesia is resumed and the patient put in the laparotomy position, the labia carefully cleansed and the anus covered by dental rubber dam or sterile towel. The cervix is inspected with a drop-light, retractors are introduced and an assistant makes pressure on the fundus and the anterior lip of the cervix is brought to the vulva; for grasping the cervix, old-fashioned sponge holders are better than tenaculum forceps. The rim of the cervix is readily examined, sometimes while the placenta is within the cervix, where it falls over the placenta as over a distended Voorhees bag. Minor lacerations are ignored. Extensive lacerations are often found without hemorrhage; they usually occur at the extreme left or right side of the rim of the cervix, extending into the base of the broad ligament; they involve the vault of the vagina. Sometimes a transverse tear or cut of the anterior lip, parallel to the rim of the cervix, is found, caused by the pinching of this part between the hand and the pubis. If the inner surfaces of the cervix be inspected, tears may be discovered produced by the rubbing action of the head as it is moved outward in delivery. Tears in the upper end of the vagina are not infrequent and are not detected by the usual method of separating the labia and looking at the perineum; they are often difficult to repair, but with the patient under an anesthetic much can be done to prevent the adhesions which often form between the cervix and vaginal tissue if such tears are not closed

by suture. The upper vagina is often torn in the performance of obstetric operations; these tears involve the midportion of the lateral vaginal wall; they are readily closed, with good results. To inspect vaginal injuries pressure on the fundus is removed, the cervix holder taken off and firm pressure is applied to the cervix, pushing the entire uterus upward, thus smoothing out and distending the relaxed vaginal vault; vaginal retractors aid greatly. There is no danger of closing the cervical canal so closely as to interfere with drainage; the extreme lower rim of the cervix is so thin that it would not unite if sutured. The last stitch is placed from one-third to one-half inch from the edge. In closing tissues high up it is often of advantage to place the lower one first, using it as a tractor to expose the upper laceration. Tears of the anterior segment are not uncommon and should be detected and repaired; this is especially true of those of the subpubic region. In repairing the pelvic floor and perineum, sutures of catgut should be employed; tears should be thoroughly brought together. The good results of closing the cervix have been seen in a small number of cases of subinvolution and retroversion. In order to prevent retrodisplacement, patients should lie early on the abdomen, and on the tenth or twelfth day begin the knee-chest posture. In 350 confinements the cervix and upper vagina have been examined in 180. Multipara with known old lacerations are not examined if infection was considered present; no such manipulation was practised. In the 180 cases the cervix needed repair in 51, and in 9 of these there was some good reason for not performing the operation. Of 43 repaired at delivery, 7 were unsuccessful, about 16 per cent.; the remainder gave excellent primary union. There was one infection in the entire series of 180; this patient was subjected to prolonged uterine manipulations, both manual and instrumental. The use of gas has been a great help in these cases to get primary union. Vaginal examinations during labor should be entirely avoided or limited as much as possible. The cervix should be immediately inspected after labor and repaired if necessary, and this procedure reduces subinvolution and uterine displacement. In lacerations of the second degree of the perineum and pelvic floor the use of upward suture of catgut permits accurate closure and restoration of the parts. Lacerations in the posterior segment of the pelvic floor are more successfully repaired than those in the anterior, hence the obstetrician should avoid pressing against the anterior vaginal vault in delivering the head.

Painless Childbirth and Safe Conduct of Labor.—SCHWARTZ (*Am. Jour. Obst.*, January, 1919) gives the results of his study of 1000 cases of labor, both ward and private patients, who received the same care. The anesthetic and analgesias employed were chloroform, ether and nitrous oxide. Scopolamin, morphin and narcophin were used in a few cases and chloral hydrate was employed in a few cases of eclampsia; ethyl chlorate in only 4 cases by itself, but in a large number of cases in connection with scopolamin-narcophin treatment. These substances should only be used when the obstetrician is in constant attendance at the bedside of the patient; or it is often desirable to use several of these agents in succession. Nitrous oxide and scopolamin, he states, are comparatively harmless for mother and child; chloroform and ether

are not so harmless for the mother and distinctly dangerous for the child, while the same statement applies to morphin. These substances when used by a competent obstetrician do not tend to produce postpartum hemorrhage. He believes that pituitrin used before delivery and ergot employed after make it possible to regulate the uterine contractions during labor and prevent postpartum relaxation of the uterus. In these cases 10 per cent. receiving no anesthetic of any sort, as they did not require it, were seven children stillborn and one died soon after delivery, making 10 per cent. fetal mortality among mothers who received no anesthetic. Chloroform was used exclusively in 377 cases (or 37.7 per cent.), of whom 115 were primipara and 262 multipara. Chloroform is most dangerous to fetal life, causing profound asphyxia; 11 children were stillborn under chloroform and 9 so deeply asphyxiated as to require artificial respiration, with 17 fetal deaths, or a mortality of 4.5 per cent. Ether was given exclusively in 54 cases, mostly toxemia and eclampsia; it was used when chloroform seemed contra-indicated; it often affects the fetus. The mortality rate among the children was 16.6, but these children were born in cases already complicated by severe maternal disease. Nitrous oxide and oxygen were used in 69 cases. In 1880, at Petrograd, Klikowitsch used this anesthetic extensively and published his result in the following year; American physicians have recently used it extensively; it is especially useful for multiparous women, and is said to be without danger. With each pain the patient is requested to take from four to six deep inhalations and the gas is then shut off before the uterine contraction has reached its height. It is contra-indicated in valvular disease of the heart, high blood-pressure and very feeble individuals. Expense may be saved by machines so contrived that an anesthetic is constantly rebreathed by the patient while the carbon dioxide exhaled is removed by passing the gas through a tank filled with sodium hydrate. This saves over 50 per cent. of the expense. The fetal mortality in these cases is 6 per cent. Scopolamin-narcophin was used in 393 cases, with a fetal mortality from asphyxia of 4.6 per cent. Experiments with scopolamin, morphin, narcotics and narcophin show these drugs act directly on the muscle fibers of the bronchials in newborn children and the respiratory centers are depressed and there is bronchoconstriction. The writer has used scopolamin and narcophin and occasionally hyocin in place of scopolamin. Narcophin must be used in larger doses, about three times the dose of morphin. When using scopolamin-morphin in the usual way the writer confines it to the first stage of labor only. The initial dose of scopolamin is $\frac{1}{130}$ grain for the average women, $\frac{1}{200}$ for smaller women; with this is given $\frac{1}{2}$ grain narcophin or $\frac{1}{6}$ grain of morphin. This is deposited under the skin, where it will be slowly absorbed. A second injection is usually given forty-five minutes after the first, and when the complete dilatation is present, scopolamin is stopped. The test for the influence of scopolamin is the request that the patient touch the tip of the nose with the index finger while the eyes remain covered. Most patients do not require more than three injections and no more is given after the cervix is completely dilated. Where labor is prolonged by premature rupture of the membrane, this method seems to be useful. When the head is on the pelvic floor in primipara a small quantity of chloroform is

inhaled. Great care must be taken that patient is not overly affected. In multipara pituitrin is often given during the second stage. Where the patient shows idiosyncrasy against scopolamin, chloral hydrate in 30- to 40-grain doses is given by rectum.

GYNECOLOGY

UNDER THE CHARGE OF

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Ovarian Function after Hysterectomy.—The purpose of a contribution to this subject by RICHARDSON (*Surg., Gynec. and Obst.*, 1919, xxviii, 146) is to present an analysis and impartial estimate of the existing evidence for and against retention of ovarian tissue after hysterectomy. Such a study seems both timely and desirable for two reasons: (1) because our knowledge of ovarian function has been substantially increased during recent years, chiefly through the intensive study of endocrinology, and (2) because there has arisen a sharp division of opinion among those most competent to decide this matter. One group is persistently advocating the routine conservation of healthy ovaries after hysterectomy, while a minority is vigorously condemning the practice as scientifically without justification. From his review of the subject Richardson concludes that the ovary is a glandular organ of complex function, our knowledge of which is at present far from complete although we do know that the uterus is not essential to a continuance of ovarian function, except as regards menstruation and reproduction. The advocates of total ablation have not furnished convincing evidence of the correctness of their contention since the disturbances of ovarian function attributed to hysterectomy are partly those associated with normal menstruation and partly those arising from damage to the ovary through operative trauma or disease. In a word, the weight of evidence furnished by anatomical, experimental and clinical investigations is overwhelmingly in favor of retention of sound ovaries both before and after the menopause age.

Non-gestational Tubal and Ovarian Hemorrhage.—Without careful study of ovarian and non-pregnant tubal hemorrhage, one might think that its occurrence was so rare as to be a novel or grotesque condition, but careful analysis of abdominal surgical work, including microscopic study, has demonstrated to BOVÉE (*Surg., Gynec. and Obst.*, 1919, xxviii, 117) that it is not a rare condition and he has made another contribution to this most interesting subject. Some of the causes that have been reported in connection with this condition are trauma, the ingestion of poisons of various kinds, the ingestion of oxytoxics and emmenagogues to interrupt a supposed pregnancy, especially when it did not exist, inflammatory changes and other pathological conditions including

neoplasms and maladjustment of the internal secretions at puberty. Hemorrhages from the Fallopian tube may occur from general conditions that similarly affect other tissues and venous stasis from circulatory disturbances or pressure from tumors may be reasonably included in a list of causes. In considering ovarian hemorrhage, it should be remembered that the hemorrhage may be confined within the ovary, constituting one or more hematomata or it may take place into the peritoneal cavity, producing, if abundant, an hematocele. In the former variety it may occur in the stroma, into new growths or into follicles in any state of development. If before or during follicular hemorrhage rupture of the follicle or of the wall about a stromal active hemorrhage occurs, the peritoneum may be deluged. Slight hemorrhage from the follicle is regarded as a normal incident of ovulation, but the loss of more than a slight amount of blood in this manner must be regarded as pathological. These ovarian hemorrhages nearly always occur during menstrual life. Non-gestational tubal hemorrhage probably has no diagnostic symptom or symptom-complex and the symptoms of ovarian hemorrhage are by no means distinctive. They vary from none known in cases of infancy found at autopsy to those at puberty resembling very closely dysmenorrhea of ovarian or cervical origin and even to those severe attacks that have caused death or led to emergency abdominal sections. Usually a history of sudden exertion that indirectly influenced the pelvic region has been followed by a very severe degree of pelvic pain, paroxysmal or quite continuous. Sometimes the pain is referred to the umbilicus or epigastrium, gradually limiting itself to the affected iliac fossa or lower abdominal zone, vomiting and collapse soon following. In some cases the pain has been well distributed throughout the abdomen and pelvis and general tenderness and muscular rigidity of the whole abdomen are usually present. Vagino-abdominal examination reveals great tenderness about the appendages. In but few cases, however, have correct diagnoses been made before operation or autopsy. The treatment of this condition consists of rest and the administration of anodynes in the milder cases while in the severer forms of the disease the same rules apply as are employed in treating ectopic pregnancy.

Removal of Intestines during Curettage.—From time to time the literature presents the history of a case in which intestines are accidentally removed by an operator during the performance of a uterine curettage. Such cases usually occur when the patient is in the puerperal state, at which time the uterus is very soft and offers very little resistance to any instrumentation. Aside from the medicolegal standpoint of such an accident, such an occurrence always causes much speculation in regard to the amount of force that must have been expended by the operator in getting into such a difficulty. Some experimental work upon the cadaver has been done by Ill (*Am. Jour. Obst.*, 1919, lxxix, 29) in order to have a better understanding of the factors operative under these conditions. His work has demonstrated that any portion of the bowel can be pulled away by traction with a forceps through a rent in the uterus or vagina and that the point of separation will be the junction of the bowel with the mesentery, although in some subjects the separation will be extraperitoneal in large measure.

The one important point about this accident from a medicolegal standpoint that these experiments have demonstrated is that the mesentery cannot be pulled away from its origin at the spine, no matter how much traction is applied, but the point of separation will always be at the junction of the bowel with the mesentery.

Tuboövarian Suppuration.—It is commonly considered that the chief or only path by which pelvic pus from tuboövarian suppuration seeks to escape is through the posterior vaginal cul-de-sac or pouch of Douglas, and indeed this is its most frequent course. However, GREEN (*Boston Med. and Surg. Jour.*, 1919, clxxx, 179) states that not infrequently deep pus, either in or around the tube, may be reached surgically by this route before definite fluctuation is obtained, and in his experience the most useful early indications of the presence of pus are persistent high temperature and leukocyte count in spite of the usually successful palliative measures of ice, elevation and catharsis, increasingly acute tenderness in the mass of exudate behind the uterus, edema of the recto-vaginal wall and ballooning of the rectum. When any three of these signs are present, he believes that it is often wiser to go in search of pus and establish drainage through the posterior cul-de-sac without waiting for positive fluctuation than by such delay to allow the patient to suffer from protracted toxic absorption. If this is not done the inflammatory process may extend upward into an iliac vessel and pylephlebitis occur, terminating in death. After the drainage of an abscess or tube, the inflammatory process generally subsides sufficiently to permit subsequent safe laparotomy, or may even recover without sufficient residua to demand further surgical intervention. Merely because tuboövarian suppuration usually points to the posterior cul-de-sac should be no reason for overlooking the other avenues by which it may escape. The pelvic abscess which accumulates in the pouch of Douglas may equally well point or be evacuated through the rectum as through the vagina. For this reason, rectal or combined examination with the fore and middle fingers should never be omitted. Other sites in which pus may point are the inguinal canals and through the linea alba, and Green cites cases of each type and urges palliation first, followed soon by drainage if unrelieved.

Ectopic Pregnancy.—Critical analyses and collective reviews on this most interesting subject almost always invite the attention of any physician and for this reason the recent review of the gynecological material and records at the Johns Hopkins Hospital by WYNNE (*Bull. Johns Hopkins Hosp.*, 1919, xxx, 15) is of interest. Of the 22,688 patients admitted to the service during the past twenty-seven years, there were 303 cases of extra-uterine pregnancy, an incidence of 1.3 per cent. The youngest patient was a fifteen-year-old white girl, the oldest was a forty-five-year-old negress. Sixty-one per cent. of the cases occurred in patients between twenty-four and thirty-three years of age, 7 patients were under twenty and 10 were over forty years old. The most common causes for which the patients sought medical attention were pain (84 per cent.), bleeding (31 per cent.) and tumor (7 per cent.). A history of abdominal pain was obtained from 300 patients, the other 3 patients stated positively that there had been no abdominal

pain or discomfort and each of these 3 patients presented an unruptured tubal pregnancy without any evidence of clot or free blood in the peritoneal cavity, therefore the common appearance of pain as a symptom in this condition is most probably caused by the irritation of blood in the peritoneal cavity. The onset of symptoms may be acute without other prodromal symptoms, although there is usually a history of a missed period or of irregular bleeding. In a second type there is an acute attack following prodromal symptoms, which the patient sometimes ascribes to her pregnancy. A third type of patient gives a history of gradual onset without an acute attack. Recurring attacks of pain occurred in 34 per cent. of the cases; some patients complained of soreness and tenderness rather than of definite pain. In several instances the pain was of several years' duration, generally with a recent exacerbation, but in each instance at operation some other condition, usually chronic pelvic inflammatory disease, was also present. Thirty-four per cent. of the patients stated definitely that they had missed one or more periods and 10 per cent. said that their last period had been overdue for from one to five weeks, while 17 per cent. had noticed that the last period was abnormal in some other respect. Nausea and vomiting occurred in a few cases, as in normally pregnant women and the patients with these symptoms considered themselves pregnant. In the great majority, however, there was a history pointing to intraperitoneal hemorrhage before nausea or vomiting had occurred. In no case was a positive Hegar's sign recorded, vaginal cyanosis was not marked in any case and Wynne believes that most cases of tubal pregnancy show no very definite gross changes in the cervix and uterine body, unless the fetus is living. Abdominal tenderness is frequently absent but pelvic tenderness is usually marked, especially when the pelvis is filled with recent clots. The temperature on admission to the hospital was less than 101° F. in 91 per cent. of the cases, but the majority of patients showed some increase in both pulse-rate and temperature. The correct diagnosis was made before operation in 46 per cent. of the cases, in 33 per cent. of the cases the condition was not diagnosed, while in the remainder of the cases, ectopic was either suspected or diagnosed while the patient was under anesthesia prior to being operated upon. The classical case of an acute ruptured ectopic pregnancy is usually clear if a satisfactory history can be obtained, but there are a great many cases in which the history points equally well to pelvic inflammatory disease. The latter disease also gives symptoms that not infrequently strongly suggest extra-uterine pregnancy. Concerning the method of treatment that was applied in this series, the study showed that laparótomy by the abdominal route was preferred in all cases except those in which there was a pelvic hematocele with symptoms and signs indicating infection. In such cases, pelvic puncture and drainage is usually a safer procedure, although a secondary laparotomy may be necessary later for continued pain. The convalescence is usually more satisfactory when a careful peritoneal toilet is performed and all blood clots removed, provided that the condition of the patient warrants the expenditure of time, but irrigation of the peritoneal cavity has been discontinued. Drainage is not employed unless there is some evidence of infection in the pelvis or a general ooze following the release of adhesions. It is interesting to note that tubal rupture occurred in 61 per cent. of the

cases, tubal abortion in 19 per cent., while in 20 per cent. of the cases the gestation was unruptured. Of 96 patients in whom there was a possibility of pregnancy after the operation, 36 have since become pregnant one or more times and 61 pregnancies have resulted in 37 full-term children. In 16 cases the pregnancy ended in miscarriages and 6 patients had a second extra-uterine pregnancy.

Tuberculosis and Cancer. — The theory prevailing among the majority of physicians for a number of years, and still prevailing among a few, that tuberculosis and malignant neoplasia are antagonistic, has not been borne out by facts, according to BRODERS (*Jour. Am. Med. Assn.*, 1919, lxxii, 390), of the Mayo Clinic, who has devoted his attention to a consideration of this subject. He states that the fact that some tissues or organs are, to a certain degree, immune from one or the other or both of these diseases does not prove that the two diseases are antagonistic. If the observations of Naegeli are correct, in which he showed that in 93 per cent. of 420 necropsies on adults more than eighteen years of age, either active, latent or healed tuberculosis had been present, then it is reasonable to believe that similar findings should prevail in an equal number of persons who have died with malignant neoplasia. Furthermore, it would seem that the reason that pathologists are not finding tuberculosis more frequently at necropsy in persons who have died from malignant neoplasia is that the pathologists are satisfied to find the malignant neoplastic condition, and therefore fail to make a thorough search for tuberculosis. Since the surgical pathologist's examinations are limited to the tissue removed by the surgeon, he is greatly handicapped in the search for the two conditions associated, while the pathologist doing a necropsy has access to a large part or the whole of the body. The fact that active tuberculosis occurs most frequently in persons under forty-five years, and malignant neoplasia, especially epithelial tissue malignant neoplasia, most frequently in persons over forty-five, does not prohibit the association of latent and healed tuberculosis with malignant neoplasia, and, as a matter of fact, in the series of twenty cases that the writer studied the two conditions were associated in the same microscopic field seven times (35 per cent.).

DERMATOLOGY

UNDER THE CHARGE OF

MILTON B. HARTZELL, M.D.,

PROFESSOR OF DERMATOLOGY IN THE UNIVERSITY OF PENNSYLVANIA.

A Positive Wassermann Reaction in Some Tuberculous Affections of the Skin. — SCHAUMANN (*Ann. de dermat. et de syph.*, 1918–19, No. 1) has obtained a strongly positive Wassermann reaction in two cases of tuberculide, including under this term erythematous lupus.

The first case was a woman, aged thirty-eight years, who presented two patches of erythematous lupus on the cheek, along with swollen lymphatic glands; she gave a strongly positive Wassermann reaction. Three years later she was seen again, when, in addition to the erythematous lupus, she presented ulcerating nodules on the legs, the papulonecrotic tuberculide; again the Wassermann was strongly positive. Intramuscular injections of gray oil were without effect upon the ulcerating lesions of the legs. The second case was one of papulonecrotic tuberculide, and in this case there was likewise a positive Wassermann reaction. The author was quite certain that neither of these patients was syphilitic. (It may be observed here that not all authorities are agreed as to the tuberculous character of erythematous lupus.—M. B. H.)

Pediculosis Pubis Due to the Head Louse.—NICOLAS and MASSIA (*Ann. de dermatol. et de syph.*, January, 1916) have observed an example of pediculosis of the pubic region, due to the pediculus capitis. As is well-known, it is rare for the various species of pediculi to be found outside their normal habitat, although the pediculus pubis is found occasionally on the axillary hair. The authors have found but a single case similar to their own in literature. Lydston some years ago reported a case of pruritus vulvæ in a young girl which was found to be due to the pediculus capitis.

Dermatitis Coccidiosa. — SEILIN (*Med. Record*, March 1, 1919) reports, from Chicago, a new case of this most interesting dermatosis. The patient was a cigar maker, aged thirty-two years. On the right palm, at the base of the thumb, was a dry scaly area, about 2½ inches square, which contained a number of painful fissures, with thickened edges, and about a dozen deep-seated vesicles. Scattered about this patch were a number of very small superficial abscesses. Microscopic examination of the contents of the vesicles revealed the presence of hundreds of coccidia. The affection had begun nine years before, with the appearance of a few hard papules in the palm, accompanied by intense itching. The treatment consisted of the application of a 1 per cent. solution of copper sulphate after opening the vesicles, the internal administration of potassium iodide and hypodermic injections of emetin hydrochloride. The effect of the treatment was remarkable; within twenty-four hours improvement was noted and within five days the patch was completely healed.

An Unusually Extensive Case of Symmetrical Keratodermia.—VILVANDRÉ (*British Jour. Dermatol.*, October–December, 1918) reports an extraordinary case of keratodermia recently under his observation in the London Hospital. The patient was a girl, aged five years, who presented no other abnormality than the condition of the skin. According to the statement of the mother the skin was apparently normal at birth, but the affection appeared soon after. The hands, forearms, elbows, knees, lower portion of the legs and the feet presented extensive areas of greatly thickened skin, with wart-like surface and some hypertrichosis. They were grayish black in color, symmetrically situated and presented the same shape on both sides. Those on the knees were

lozenge-shaped, ending in a point some distance below the patella. The palms and soles were markedly affected and deeply fissured, presenting a bark-like appearance. There was no history of any hereditary factor. Some excellent photographs accompany the paper which illustrate the features of the case better than any verbal description.

Acute Lichen Planus Treated by Lumbar Puncture.—PERNET (*British Jour. Dermatol.*, July–September, 1918) at a recent meeting of the Dermatological Section of the Royal Society of Medicine presented a case of acute lichen planus which had been treated by lumbar puncture. The patient was an ill-nourished woman, aged fifty-four years, in whom the disease had lasted two months and was accompanied by an irritation which the patient described as "dreadful." A lumbar puncture was done and 8 c.c. of spinal fluid removed; the severe pruritus was relieved and the eruption became pale and began to undergo involution. This was the exhibitor's third case thus treated, and in all he had obtained good results. In the discussion which followed the presentation of the case, Pringle stated that he had employed this procedure several times, always with very satisfactory results as to the relief of the itching, but in a few days it recurred and he had not considered it advisable to make a second puncture. Bunch agreed that the treatment relieved the itching, but he did not find that it benefited the eruption.

Multiple Benign Basal-cell Epithelioma of the Scalp. — ADAMSON (*British Jour. Dermatol.*, July–September, 1918) reports a new case of this affection and briefly refers to some of the cases previously reported as endothelioma capitis. The patient was a man, aged sixty-one years. On the scalp were numerous, forty to fifty, small tumors varying in size from a hemp-seed to a chestnut. They were quite firm, the color of the skin, freely movable and devoid of hair; there were also a few small lesions of a similar character on the back. The tumors on the scalp had been present for twelve years, but those on the back had been noticed for thirty years. Sections made from an excised tumor showed the features characteristic of benign basal-cell epithelioma. The author agrees with Dubreuilh and Auche that the cases of multiple tumors of the scalp which have heretofore been described as endothelioma capitis are actually basal-cell epithelioma belonging to the same group as the epithelioma adenoides cysticum of Brooke. Like this affection, it shows a marked tendency to occur in two or more members of a family. According to Dubreuilh and Auche there are no authenticated cases of endothelioma capitis.

HYGIENE AND PUBLIC HEALTH

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Epidemiology of Cerebrospinal Fever at the United States Naval Training Station, Great Lakes, Ill.—SHORT (*U. S. Naval Med. Bull.*, October, 1918) states that epidemic cerebrospinal fever is a disease caused by the meningococcus, which is spread for the most part by direct contagion from patients and healthy individuals. In military organizations the meningococcus has a predilection for young recruits, but is usually inert in the absence of depressing or resistance-lowering factors. The arguments for isolating meningococcus carriers to prevent the disease are not convincing, since consistent practice on that basis has proved not only extravagant and against military efficiency, but also impracticable and non-effective. The search for meningococcus carriers and their disposition should not cause neglect of the more generally effective and easily controlled measures of hygiene, of which the following are of greatest importance: The prevention of crowding among young recruits; the allowance of ample time for their "hardening" and "seasoning;" protection from weather, overwork and fatigue, and the use of all measures that will promote the general health of the camp.

Winter Hibernation of Anopheles Larvæ.—GRIFFITHS (*Public Health Reports*, November 15, 1918, No. 46, xxxiii) states that anopheles (crucians and punctipennis, at least) pass the winter in the larval stage. That is true for northern Louisiana (for crucians) during a severe winter for that section. Evidence, though less conclusive, shows that punctipennis, at least in the larval stage, withstand a severe eastern Virginia winter. Apparently pupation does not occur at low temperature, or until ordinary room temperature obtains. In selected places considerable numbers of anopheles larvæ pass the winter as such. Larvacides should be applied in the fall sufficiently late to kill the last batch of larvæ, or before season suitable for the completion of their aquatic stages in the spring.

Sanitation of Swimming Pools.—SMITH and SCHOBERG (*Am. Jour. Pub. Health*, June, 1918) state that swimming pools should be so well lighted that a submerged person can always be readily seen. Economy, therefore, suggests locating the pool at the top of a building. The waste water from the pool can then be used for flushing of closets, urinals, etc., in the building. The sides of the tank should be smooth. Four sides of the pool should be available for use, with life-rails all around.

Overflow gutters are necessary, and there should be a trip basin twelve inches below the main platform. When the tank is emptied the sides should be scraped, scrubbed and flushed, then steamed, aired and dried. Wreaths of sediment on the floor should be removed and pumps on the general plan of a vacuum cleaner are recommended. Refiltration and constant agitation of the water should prevent formation of wreaths. The water selected for the pool should be the cleanest available and not that whose source is simply the most accessible. Constant refiltration makes it possible to use a given filling a greater length of time. This is an important item in cost of maintenance and will more than compensate for the initial cost of the equipment. The tendency toward installing a plant of too small capacity should be avoided. It should be possible to refilter all the water in the tank in one day (eight-hour days are in vogue). Usual frequent attention should be given to reversal of filters, washing and steaming. Dilution should be practised sufficiently to make up the loss by splashing, etc. No definite amount can be stated. This should depend on the number of bathers, frequency of refilling, etc. As a rough working rule, it is suggested that the dilution be sufficient to amount to one filling between refillings. Refillings should be determined by the number of bathers, size of pool, and bacterial content as there is no direct relationship between the number of weekly refillings and the sanitary condition of water. The general appearance of the water counts for nothing. Both calcium hypochlorite and copper sulphate have advantages, the latter probably being the favorite for chemical disinfection. Either should be used in strengths increasing from 0.5 part to 1,000,000 of water, depending on the size of the pool, number of bathers, the hardness of the water, and the bacterial reduction obtained. Bleach must be tested frequently for available chlorine. It quickly disappears from the pool. Full shower bath with soap should be demanded of all bathers. To make this possible the shower apparatus must be inspected very frequently. Instruction should be given bathers in the purpose of the bath. Especial attention should be given to the perineal region. When water strikes a person's body the natural tendency is to urinate. This should occur in the shower, not in the pool. The floor should be taken care of to prevent tracking the dirt, bacteria, etc., which have been washed off by the shower, onto the deck about the pool. On the pool platform inspection of every entrant should be performed. Bathers should wear no clothes. If this be impracticable, the authorities of the pool should furnish the suits—one-piece, undyed, scanty—and see that they are properly sterilized and dried between using.

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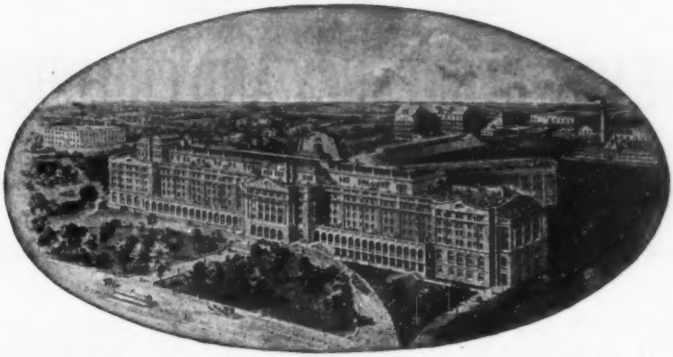

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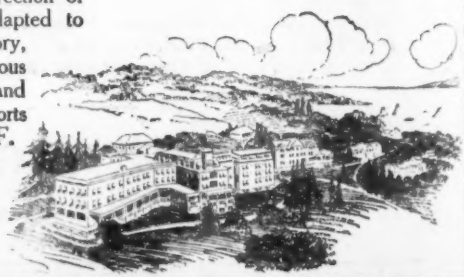

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